THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

NOVEMBER, 1907.

ORIGINAL ARTICLES.

GASTROMOTOR INSUFFICIENCY DUE TO PERIGASTRIC AND DUODENAL ADHESIONS.

By Frank Billings, M.D.,

PROFESSOR OF MEDICINE IN THE RUSH MEDICAL COLLEGE, AND THE UNIVERSITY OF CHICAGO, CHICAGO, ILLINOIS.

Motor insufficiency occurs when there is a loss in equilibrium between requisite labor and power of labor. When the motor power of the stomach is not sufficient to meet the demands made upon it, the viscus will discharge its contents partially only, or it will become entirely empty only after a prolonged period of time.

There are two fundamental causes of gastromotor insufficiency: (1) A deficient muscular tone or atony, which may be called also a myasthenia; and (2) mechanical hindrance to the expulsion of its contents.

Atony of the gastric muscularis is common. The condition may be hereditary. It may occur or follow the severe infectious disorders. It may be present in the anemias and in cachectic and malnutritional conditions. It is present in neurasthenic and psychasthenic and neurotic conditions. Atony without dilatation does not usually present evidences of motor insufficiency of a degree to produce stasis of stomach contents, but dilatation may occur readily with atony under conditions which require a greater power of labor. If too much food is taken at times; if food is eaten too hastily; if there be congenital defect, like gastroptosis; if slight mechanical hindrance be added in the form of adhesions anywhere in the gastro-intestinal tract; if an abnormal tonus of the pylorus occurs from hyperacidity, so often present in neurotic conditions, dilatation may be added to atony.

In the second group with mechanical hindrance, which is usually due to a stenosis of the pylorus, from the many causes of that condition, the power of the gastric muscularis may be normal or even hypertrophic. But with the mechanical hindrance the gastric muscle is incapable of expelling the ingesta, and dilatation and stasis result.

The motor function of the stomach is very important in the digestive process. Motor and secretory power of the stomach are directly related. Normally, acid chyme, passing through the pylorus, excites the secretion of the intestinal and pancreatic juices. It also excites a nervous reflex which closes the pylorus after a certain amount of the acid chyme has passed into the intestine. With lessened acidity of the stomach contents, or with anacidity, it is found that the stomach empties itself much more rapidly than if the chyme were acid. In some instances, if the stomach is loaded with an enormous amount of food, this antacid condition will permit such an enormous quantity of food to pass from the stomach into the intestine in a short time that the intestinal digestion is inadequate to take care of the food, and diarrhœa results. On the other hand, with hyperacid conditions of the stomach, the food may be retained too long, because but a small amount of very acid chyme will be tolerated in the duodenum, and the duodenal reflex keeps the pylorus in a state of spasm. In the latter condition, with atony of the stomach, as in neurotic conditions, there will be a relative insufficiency with or without dilatation.

The symptoms of motor insufficiency depend upon the degree of insufficiency. In atony of the stomach there may be delayed expulsion of the stomach contents, manifested by a sense of epigastric oppression and weight; and the presence of gas or air, with a bloating of the abdomen and eructations of gas. The patient feels frequently as if the stomach were overloaded when but little food has been taken. If the stomach is tested with an Ewald meal, varying degrees of reaction as to the acidity will be found. Upon a full meal of mixed character, and especially if it contain indigestible particles like seed and leaves of vegetables, a remnant of these indigestible things will be found in the stomach after the physiological time of about seven hours, when the stomach should be empty. After a full meal at night the fasting stomach of the morning will be found usually empty.

With severe motor insufficiency due to atony and dilatation, the objective symptoms are oppression and weight after eating, with bloating with gas and belching, burning in the epigastrium, and indefinite pains dependent upon the nervous condition of the individual. In some instances there will be vomiting of food that has remained in the stomach for an abnormal length of time. This vomitus may show decomposition with the presence of organic acids, various bacteria, and varying degrees of normal HCl and

the ferments. An Ewald test meal may show normal acidity or may show lessened or increased amounts of HCl and varying degrees of pepsin and rennin digestion. There may also be present lactic or other organic acids; bacteria of various kinds, with yeast cells; and, if there be hyperacidity, sarcinæ may be found. A large meal of mixed character will show at the end of seven hours the presence of food particles, with the reactions and other conditions present after the Ewald meal. Leukocytes are usually present, and are usually undigested. The fasting stomach of the morning, after a heavy meal at night, will usually show in this severe degree of insufficiency the presence of food with more or less normal gastric juice, containing in some instances organic acids, bacteria, and leukocytes. Unless there be some lesion of the stomach, there is no blood, either microscopic or occult.

If there is an atony of the stomach with dilatation, distention with gas will reveal it. This distention does not cause pain, and there are usually no peristaltic waves to be seen.

If the high degree of motor insufficiency is due to mechanical hindrance at the pylorus, the same findings may result with test meals and upon chemical and microscopic examination. If there is present a chronic ulcer, or the ulcer of an advanced neoplasm, visible and occult blood will be found in the stomach contents and in the stools. If there is cancer, the Gram-proof Oppler-Boas bacillus usually will be found. If the chronic ulcer is present, there may be found leukocytes in excess, and some of them digested. If the stomach is distended with air or gas, and if the disease causing the stenosis is an ulcer, either chronic or that due to a neoplasm, or if there exist recent perigastric and duodenal adhesions, the inflation of the stomach will cause pain, with sometimes a board-like contraction of the stomach, from which the patient gets relief by eructations of the gas or by vomiting. In this condition, too, frequent peristaltic waves may be seen passing from left to right through the epigastrium.

If there be a severe degree of insufficiency with stasis, the amount of fluid absorbed into the blood stream is small, and, in consequence, constipation with dry stools, and a diminution of the twenty-four-hour urine excreted result.

Between this high degree of insufficiency and the slight insufficiency which may be called relative, there are varying degrees of the condition which may, however, be recognized if the patient be observed for a long-enough period of time and if the motor power of the stomach is studied by the proper test meals. A study of the motility, with test meals, should always include the Ewald meal, to ascertain the secretory power of the stomach, as well as a large mixed meal, which should be studied not only seven hours after it is taken, but also the condition of the fasting stomach should be ascertained in the morning after a heavy meal the night before.

Perigastric and duodenal adhesions may cause motor insufficiency. These adhesions are most frequently due to cholecystitis. Chronic ulcer of the stomach or the duodenum may also cause adhesions, but ulcer of the stomach is more apt to interfere with its motility by causing pylorospasm or by producing scars which deform the organ. Adhesions due to operations upon the organs involved may also leave adhesions. Adhesions which result from other pathological conditions, like tuberculosis of the peritoneum, typhoid fever, and other ulcerative conditions, are not, as a rule, situated in the region of the stomach and duodenum, and are not, therefore, to be considered in this paper. Perigastric adhesions produce symptoms that may be classed as acute or chronic, depending upon the age of the adhesions.

The patient who has acute adhesions in the region of the gall-bladder, duodenum, and pylorus, suffers, as a rule, from active manifestations of the disease which causes the adhesions. As I have stated, this is most commonly cholecystitis. Therefore, the patient has pain in the epigastrium, which usually centres upon the right side under the costal arch. With this pain there is a circumscribed tenderness upon palpation, and this is very acute if percussion is made upon a small pleximeter, like the point of the finger. When food is taken, pain of varying degree results. Not infrequently vomiting occurs after taking food, with the relief of the pain. If the infection is confined to the gall-bladder, there is no jaundice. If the infection reach the larger ducts, with or without gallstones, there may be jaundice. Associated with the local symptoms there is usually general disturbance in the form of rigor, more or less fever, rapid pulse, with some physical prostration. If the stomach is distended with air or gas the pain is usually severe and is referred to the gall-bladder region, and the tenderness mentioned above is aggravated. Not infrequently the stomach is tonically contracted and is felt board-like under the hand.

If test meals are given, hyperacidity is usually found. It will be found, too, that in many instances the contents of the stomach are delayed in passing from the organ. There is no decomposition, however, of the food remnants, and no visible or occult blood in the stomach contents or in the stools. There is usually no excess of leukocytes.

This condition will continue for an indefinite period, but usually with the subsidence of the local infection in the gall-bladder improvement in the condition occurs, and finally the patient recovers from all of the acute manifestations. Following the acute attack, a relative insufficiency remains. The patient complains of the symptoms already mentioned in relation to simple atony of the stomach without dilatation. Usually relapses occur with new infections of the gall-bladder, and the patient passes through the same series of symptoms. The condition is not infrequently mistaken for ulcer

of the stomach or duodenum. There may be some difficulty in differentiating. In chronic ulcer of the stomach near the pylorus, or in the duodenum, there is usually hyperacidity, with a tendency to increased tonus of the pylorus. In some instances pylorospasm may occur, with pain and symptoms so like those enumerated in cholecystitis with adhesions that they could not be differentiated by a consideration of the symptoms alone. With ulcer, however, the stomach tests will usually show, not only hyperacidity, but the presence of occult blood and sometimes visible blood in both stomach contents and the stools. There are also present numerous leukocytes, many of which are digested. If there is much stasis with hyperacidity, sarcinæ are present. The main differentiating point is the presence of blood and the more constant presence of hyperacidity than in cholecystitis with adhesions. Chronic ulcer, like cholecystitis with adhesions, usually has periods of acute manifestations, followed by periods of latency. In the latent ulcer all symptoms may disappear, but usually there is more or less motor insufficiency of the stomach. Chronic ulcer may be followed by mechanical hindrance through the development of scar tissue and stenosis of the pylorus, or by deformity of the stomach, due to scar contraction, with resulting insufficiency of high grade. This is a condition rarely if ever occurring with adhesions, and, consequently, when this stage is reached, there is only the question as to whether the mechanical hindrance is due to scar tissue from ulcer or to neoplasm.

Cholecystitis with adhesions occurs in infective cholecystitis with or without gallstones. It is known that cholecystitis occurs in the course of typhoid fever, and also during convalescence from that disease. The stomach symptoms enumerated above may occur in a cholecystitis from any of these causes, and when they occur the attention of the physician should be directed toward the probability of a cholecystitis. Motor insufficiency due to recent adhesions from cholecystitis requires surgical interference to attack the fundamental disease. Before operation is done, and while the patient is under medical care, the treatment is that usually directed to the cholecystitis. The stomach should be given absolute rest for a time. Hot applications may be made over the epigastrium, and the patient may be kept in good general condition by the use of normal salt solution, given by the rectum, to the amount of 8 to 16 ounces, every four to six hours. Operation for the cholecystitis after the acute manifestations have passed is safer than during the very acute stage.

Old adhesions about the duodenum and pyloric region of the stomach may be the result of former attacks of cholecystitis, occasionally from chronic ulcer, and often, in this day of modern surgery, from surgical operation on the organs in this region. Occasionally these adhesions are in the form of dense, scar-like tissue,

which may produce more or less mechanical hindrance by contraction and subsequent narrowing of the gut or of the pylorus, or they may contract, distort, and thus narrow the lumen of these organs. In this event the patient may suffer from insufficient motility, due to dilatation, with atony, or with an hypertrophy of the muscle of the stomach. Here there is usually no pain, but the usual symptoms of insufficiency are present, both objective and subjective. When the stomach is distended with air there is usually no pain, and relatively no tenderness, in the pyloric region. The Ewald and the motor meals may show stasis and decomposition, without any interference with the normal secretions. There is usually no blood and no excess of leukocytes, and no digestion of leukocytes. If the scar tissue is dense and tumorlike, it may be mistaken for the scar tissue of a healed ulcer, or for a neoplasm. But if there is an open ulcer, the presence of visible and occult blood, hyperacidity and sarcinæ in the one and lowered acidity and Oppler-Boas bacilli in the other, will enable one to differentiate. As I have said, these cases are very rare, and when they occur are subjects for surgical interference.

The great majority of chronic perigastric and duodenal adhesions are of the less dense variety, and are important only when present in patients who suffer from an atony or myasthenia of the stomach, due to any of the causes of atony and myasthenia. If such a patient is a neurasthenic or a psychasthenic, or is neurotic from any cause; if he suffers from any of the anemias, or has a severe infectious disease; if he is careless in his eating as to the amount, or if he does not masticate thoroughly; if he overworks, etc., he is then aware of discomfort after eating. As a rule, these manifestations are purely subjective, and are those enumerated in the earlier part of this paper. Many of these patients talk about adhesions, especially those who have had operations. They can feel the adhesions pulling, have a sense of oppression and weight, of burning and of bloating after eating. They have pain in different parts of the abdomen and elsewhere. Many of them suffer from disturbance of the vasomotor system. They may have palpitation of the heart, cold extremities, or a sense of air-hunger; they tire easily, and many of them diet themselves so closely as dangerously to reduce the general nutrition of the body. Many of them submit themselves to further operations. Occasionally the moral effect of a third or fourth operation may result in improvement for an indefinite time; but, as a rule, the secondary operations do not relieve. A careful examination of such patients will show, with the ordinary secretory test meal, varying degrees of acidity, but usually a condition not far from the normal. The normal ferments of the stomach will be found present. With the motor meal the stomach is empty after the physiological time, and the fasting stomach of the morning is always empty and clean after the full dinner of the night before.

There is, in uncomplicated cases, no abnormal thing found in the stomach contents or in the stool.

Such patients are never surgical and are always subject to improvement and cure under the measures which will improve the fundamental cause of the pain and gastric myasthenia or atony. The surgeon has now learned not to operate upon a neurotic subject with gastroptosis. He must not operate upon the neurotic who fancies he suffers because he has adhesions in the belly, the result usually of cholecystitis or of surgical operation. If such patients treated individually are given moral support, a proper mixed diet of good food, have rest with proper hydratic, calisthenic, and other personal management, they will, as a rule, become well.

I do not wish to prolong this paper by the citation of numerous cases which have come under my observation, but I shall relate one which is an example of motor insufficiency due to acute adhesions; the same individual later presented an example of a neurasthenic and neurotic subject, with subjective disturbances of motility, and submitted himself to subsequent operations without relief.

Mr. C. C., aged forty years, a native of the United States, white, presented himself to me on May 1, 1904. He was a travelling salesman, whose early history was not of importance, with the exception that he had had typhoid fever when about twenty years of age, from which he made, apparently, a good recovery. His habits were good. He had always been a large eater, and, as a travelling salesman, had in many instances eaten rapidly, and had often partaken of much pastry at railroad stations. In the fall of 1903 the patient began to have attacks of indigestion, characterized by vomiting, after hasty eating. This was associated with a sense of oppression and some pain preceding the vomiting, and each attack lasted for two or three days. Five months ago he had a severe attack in which there was a sense of distention of the stomach, belching of gas, and a good deal of pain in the epigastrium. There was nausea without vomiting. A physician passed the stomach tube and washed out the stomach and entirely relieved him. A few days after this he had slight jaundice, with discoloration of the sclera, and a continued disturbance of the stomach, with some burning in the epigastrium, oppression after eating, bloating with gas, and belching Since that attack, five months ago, the difficulty has increased, until he is in almost daily discomfort. Usually there is pain, which comes on from one to two hours after eating, associated with a sense of heaviness and with a good deal of gas, which bloats the abdomen, and is with difficulty eructated. There is tenderness over the epigastrium with the pain. He has had no chill and thinks he has had no fever.

The examination at this time shows a fairly nourished man, who states that he has lost about twenty-five pounds in weight during the last six to eight months. An examination of the mouth

and throat shows nothing abnormal. The heart and lungs appear normal. The abdomen is moderately enlarged, but symmetrical; the greater curvature of the stomach appears to reach to the umbilicus. There is considerable tenderness in the epigastrium, and especially in the region of the pylorus and gall-bladder. Upon percussion with the point of the finger as the pleximeter in this region, there is marked tenderness. Distention of the stomach, by giving separate solutions of tartaric acid and bicarbonate of sodium, causes considerable distress, and there is increased tenderness with the distention in the region of the gall-bladder. No peristaltic waves are seen, and the patient secures some relief from the distention by belching gas. After five minutes the gas can be felt passing through the pylorus. With an Ewald meal the total acidity is 98, free HCl 58, combined HCl 40, and there is a trace of lactic acid present. Microscopically, there are a few leukocytes undigested, but no blood and no bacteria. Upon a full meal, given at noon, and the stomach tube passed at 7 P.M., small food remnants were found, consisting of meat and vegetable fibers, and starchy granules. The total acidity was 65, of which 42 was free HCl, 23 combined HCl and acid salts, and there was no lactic acid. The microscope revealed no blood, no leukocytes. The patient was given a heavy meal at night, including tea-leaves and some seedy fruit. The stomach was empty upon aspiration, but there was washed out some vegetable tissue, meat fibers, and some of the tea-leaves and seeds of fruit. This wash water was acid in reaction. There was no blood in either the stomach contents or the stools. The blood examination showed 4,240,000 red cells, 82 per cent. hemoglobin, and 12,500 white cells. The differentiation of the whites showed a normal condition. The diagnosis of cholecystitis with motor insufficiency of the stomach was made, and on May 16 the patient was operated upon by Prof. A. D. Bevan. Calculous cholecystitis with adhesions to the pylorus and colon was found. Cholecystectomy was performed. Following the operation the patient had a moderate lower left-lobe pneumonia, from which he made an uninterrupted recovery. On June 15 the patient was well and able to leave the hospital, at which time a motor meal was given and in the physiological time the stomach was found entirely empty.

On March 2, 1905, the patient presented himself again. At this time he stated that following operation he had for a time been in a fair condition of health. Then he became depressed mentally, and at times he felt that he could not live. He stated that his appetite was poor, and he often had a feeling of sourness in the mouth, and belched a good deal of gas. There was no discomfort after eating, but he felt nervous four or five hours after the meal. He had not regained his strength, and when he attempted to follow his occupation he became easily fatigued and had no confidence in himself. In November, 1904, seven months after his operation for

cholecystitis, he was again operated upon by a surgeon in a neighboring State. At that time it was stated that his stomach was dilated, and he was told that adhesions were found about the region of the gall-bladder and stomach, and that the appendix was inflamed. The appendix was removed and the adhesions broken up. Ten days after operation he had severe pain under the right costal arch, and a slight wound abscess formed. After recovery from this operation he had a a sense of fulness in the upper right abdomen, and, as he stated, it felt as if it were full of adhesions. He now returned for further examinations. He remained in the hospital for one week, during which time he was given both Ewald and motor meals, with absolutely normal findings. There was no stasis in the stomach, and the secretions were normal, with the exception of moderate hyperacidity. He was advised to take a mixed simple diet of a plentiful amount, to take hot and then cold sponge baths every morning, to rub down thoroughly afterward, to go about his work, but to modify it, and not to do too much, and, above everything else, to try to forget that he had ever had any disease or operation. On June 21, 1905, three months later, the patient again presented himself, complaining of pain in the upper belly, chiefly in the region of the scar of operation. This pain was aggravated by deep pressure, by coughing, and exercise. He required a laxative every day to move the bowels. He had very little discomfort after eating, and that chiefly in the form of a sense of oppression, with the presence of a good deal of gas. A physical examination failed to reveal any evidence of disease. Stomach tests showed normal secretion and normal motility. Again he was advised to follow hygienic methods, and an attempt was made to give him moral support. On January 3, 1907, the patient again presented himself. He reported that he had remained in much the same condition of discomfort as to pain in the belly and a sense of drawing and weight. In September, 1906, he had come to Chicago and had been operated upon by a Chicago surgeon, who stated that he found adhesions about the colon, stomach, and lower surface of the liver, which he attempted to remove. Following this operation he was relieved for a time, but again the pain occurred in the upper belly, with a sense of drawing in the region of the wound. He now complained of pain in the region of the wound, of a sense of contraction and weight, which was worse when he exercised, but was present all of the time. There was very little, if any, discomfort after eating, and this in the sense of some oppression and of some bloating with gas and belching. He did not vomit. The bowels were slightly constipated. Since his operation in February, 1906, he had lost fifteen pounds. He had not worked during the last year. The physical examination at this time revealed absolutely no evidence of perceptible disease excepting the four scars in the right abdomen, three in the region of the gall-bladder and one near the appendix. He remained

in the hospital for five days, during which time his temperature was normal, pulse good, the urine normal. After a full dinner, given at 6 P.M., the stomach was found entirely empty at 7.30 the next morning. Upon an Ewald meal the total acidity was 28 without free HCl, 28 combined HCl and acid salts. Microscopic examination showed no blood, a few undigested leukocytes without bacteria. A full dinner, given at noon, showed an empty stomach seven hours later, without the presence even of gastric juice. A stool was normal, and no occult blood was found. The blood examination showed 4,600,000 reds, 91 per cent. hemoglobin, 12,300 whites.

With this condition the patient was advised that he had no disturbance of the stomach which would require surgical interference, but again he insisted upon surgical relief, and in January, 1907, was operated upon by another Chicago surgeon. It was stated that adhesions were found in the region of the old operative wounds and between the liver, stomach, colon, etc. These were broken up, and the patient made a good recovery from the operation. A letter received from him in the latter part of April, conveys the information that he has had no relief from his former sufferings.

This patient presents, as I have stated, examples of motor insufficiency due to acute perigastric adhesions and cholecystitis, for which operation was indicated, and was successful in removing the fundamental cause. But the patient was a neurotic, who continued to suffer from subjective symptoms, and, although subsequent examination showed no evidence of stasis of the stomach due to an insufficiency, he was operated upon three times more, and without relief.

Had the patient been kept under institutional treatment, subsequent to his first operation, for a sufficient length of time to restore his nervous equilibrium, he doubtless would have entirely recovered. In his neurasthenic state there can be no question that there was a general myasthenia, with atony of the stomach; consequently, he suffered from subjective symptoms of disturbed motility, and, above all, he suffered from discomfort incident to the adhesions following four operations, because his nervous apparatus was so irritable that every abnormal thing in his body gave him discomfort.

CHYLOUS ASCITES AND CHYLOUS PLEURISY, IN A CASE OF LYMPHOCYTOMA INVOLVING THE THORACIC DUCT.

By George Dock, M.D.,

PROFESSOR OF MEDICINE, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICHIGAN.

The following case seems worth recording, though incomplete in some respects, on account of the bearing it has upon the question of the relation of leukemic processes to those generally classed as

sarcomatous. The true relations cannot be made clear until the exact etiology is known, or at least until the mechanism of the leukocyte mixture is understood. Clinically and anatomically the case would fit into the classification of sarcoma. The picture is almost the same as that in a case reported by M. Herzog[1] some years ago as a lymphosarcoma. But many conditions formerly so classified have been separated on account of the peculiar condition of the blood, or of the minute histology of the new-formed tissue—chloroma, Hodgkin's disease. In this case the blood had a similar change, though the total number of leukocytes was only slightly increased. While it may be said that such cases are merely sarcomas, with accidental cells in the blood, it seems to me more rational to classify the present case as I have.

J. C. G., farmer, aged fifty-nine years, single, American, was admitted to the surgical clinic of the University Hospital, October 1, 1906, on account of an abdominal tumor and ascites, and was transferred to the medical clinic October 8.

His father died at sixty-six years of pneumonia, his mother at eighty of apoplexy. Two brothers are living. One brother died of yellow fever. A sister died of "paralysis." As a child, patient had measles, whooping-cough, varicella, and typhoid fever. Had "fever and ague once." Fifteen years ago had pneumonia; in bed six days. Later, had symptoms of empyema, followed by the formation of a swelling low down in the left side of the thorax. This "broke internally" after lasting a year, and soon after it broke blood and pus were evacuated per rectum. Six years ago a soreness came in the site of the former swelling, tender on pressure, and lasted two years. Four years ago a hard spot came in the midaxillary region, low down in the left thorax. He than noticed enlargement of the abdomen, and a tumor was discovered by Dr. W. F. Hoyt, of Paw Paw, Mich. Dr. Hoyt advised the patient to go to the hospital when he found the tumor was growing rapidly. Dyspnœa became marked, especially on lying down.

On examination in the surgical clinic, December 4, 1902, as I find in the notes kindly furnished me by Professor de Nancrède, "a mass was found extending from under the ribs on the left side nearly to the inguinal canal, and from the right nipple line to the left midaxillary line. The mass was freely movable; it had a blunt edge on the left side, and several notches in the lower edge. The mass seemed to be made up of three or four polyp-like projections." A diagnosis of abdominal tumor was made and the patient returned to his home. Soon after this many glands became enlarged in the neck, groins, and axilla. Some of them afterward became smaller. A year ago the abdomen began to get larger, and finally reached 60 inches around the waist. There was great dyspnœa. There

[1] Lymphosarcoma of the Mesentery. Jour. Amer. Med. Assoc., February 11, 1899, p. 275.

was a grating sensation in the abdomen, audible to others as well as the patient. Under treatment by salts for six weeks, the waist fell to 36 inches. The strength was much reduced by the treatment. The abdomen was aspirated in August and September, 1905, and six and nine quarts, respectively, of pink, opaque, and milky fluid, were withdrawn. Both times large quantities of fluid leaked through the punctures for several days. On admission to the surgical clinic October 1, 1906, six liters of similar fluid were removed by Professor de Nancrède, and several more liters drained through the wound, as before. The patient was then transferred to the medical clinic.

On examination by Dr. F. W. Smithies, October 8, 1906, the following notes were made (abstract): Temperature, 97°; pulse, 76; respiration, 21. Frame medium; muscles small; panniculus thin. Weight 152—about as usual. Patient lies partly on right side, propped up in bed; looks tired; voice weak. Skin cool, dry, inelastic; sallow in general; darker on face, axillæ, and arms. Slight œdema of ankles. Over most of body and extremities are numerous small papular eruptions, and scars of brown, purple, or pink color, in various stages of evolution. Scars of old papular eruptions on face. Cervical glands slightly enlarged, discrete, hard, and painless. In each axillæ are two lymph glands the size of large marbles, rising 1 cm. above the general surface. The inguinal glands are similarly enlarged. Eyes sunken, lids dark, scleræ pale with slight yellow tint; pupils equal; react slowly to light. Cheeks and ears pale; lips pale, slightly cyanotic. Tongue tremulous, pale, thick, marked by teeth; surface dry, with thin coat. All teeth gone. Neck long, thin. Thorax short, shallow, depressed below level of nipples in front and with slight funnel chest. Clavicles prominent. Interspaces retract in inspiration, especially in upper axillary regions. Litten's phenomenon in left from sixth to eighth intercostal space. On the right there is only a faint shadow in the eighth interspace. On percussion the apices are negative. Right lower lung border at fifth rib in the parasternal line. Dulness in the axillæ while lying. On sitting up the line of dulness rises to the fourth rib and extends at that level into the back, where it rises again. On the left, pulmonary resonance to the seventh rib. Slightly diminished below the clavicle. On auscultation, soft bronchovesicular breathing, with piping rales, is heard on right above the dulness; below that sounds almost inaudible. On left, harsh vesicular breathing, especially below the clavicle.

The apex beat is faintly visible and palpable in third interspace just inside of nipple. Upper border of dulness on third rib; left edge in the third interspace just outside of nipple. Right side at left edge of sternum. Sounds faint at apex. The second pulmonary accentuated. Radial artery thickened; pulse small, regular, compressible. Blood pressure, Stanton 12 cm. band, systolic, 100

100 to 104; diastolic, 55 to 62. Veins of arms, thorax, and abdomen dilated.

The abdomen, two inches above the level of the ribs, is roundish, but flattened on top and bulging on sides. Abdomen measures 102 cm. at the navel. Wall tense, resistant, especially in left iliac region. There is a hard nodular mass in the left side, extending from the right of the navel to the left posterior axillary line, and from the margin of the ribs to the left iliac fossa, filling the latter. The upper border runs down from the lower costal cartilages toward the navel. The surface is smooth in general, but with large prominences. The right side of the abdomen is resistant, but deep palpation is impossible. The edge of the liver can be felt on deep inspiration. Spleen not palpable. The mass seems continuous with its dulness in the upper part. There is fluctuation on the right side, less distinct on the left. There is movable dulness in the abdomen, more distinct in the right side.

Urine: Twenty-four hours, quantity 410, and 600 c.c.; specific gravity, 1026; turbid, alkaline (decomposed); no albumin (3 tests); no glucose; no bilirubin; sediment negative.

Blood: Flow rather sluggish; color dark, watery; red blood cells, 4,390,000; leukocytes, 8651; hemoglobin (Miescher), 70 to 80 per cent. For differential counts see below.

On October 9, I found some changes from the condition noted above: "The apex beat is under the nipple in the fourth interspace. The abdominal mass lies more in the middle of the abdomen between the two parasternal lines, and from the margin of the ribs to three inches from Poupart's ligament. It is very superficial, partly hard and nodular, partly soft and elastic. It moves slightly with respiration. The left lumbar space is soft. The lower end of the mass is thick. It gives dulness on percussion. To the right of this mass other nodular masses can be felt an deep palpation."

One of the enlarged axillary glands was removed for examination. The report (Dr. Warthin) is: "Lymphocytoma (lymphosarcoma). Aleukemic stage?"

On tapping the abdomen in Monro's point I obtained a thin, milky, slightly pink fluid, and similar fluid was obtained from the right pleura. The amount taken from the abdomen was 2450 c.c. Specific gravity, 1014. Amphoteric to litmus. Acid to phenolphthalein. It contained 3.5 per cent. of fat. Most of the pleural fluid was lost by accident, and not measured, but enough was left for examination of the sediment (see below).

The patient left the hospital before any further examinations were made. At the patient's home it was not possible to make careful observations. He failed slowly, and died January 1, 1907. Through the efforts of Dr. W. F. Hoyt, I was fortunate enough to obtain an autopsy, which was made by Dr. A. S. Warthin. I give an abstract of his notes:

Autopsy, January 10, 1907, 2.30 P.M.

Clinical diagnosis: Chylous ascites, lymphocytoma. Chylous pleurisy. Abdominal tumor—splenic(?) and lymph glandular.

Pathological diagnosis: Chylous ascites, pleural effusion, lymphocytoma of mesenteric and retroperitoneal glands. Obstruction of thoracic duct by tumor mass continuous with mesenteric tumor. Lymphocytoma infiltration and secondaries in all organs. General atrophy and passive congestion. Lymphoid hyperplasia of bone marrow.

Frame large. Abdomen greatly distended. Through abdominal wall can be felt, in left hypochondrium, a somewhat irregular tumor, extending to about median line at level of umbilicus and a hand's breadth below level of same. In pyloric region a smaller tumor mass can be felt through abdominal wall; somewhat movable, apparently connected with mass on left side. Over this several smaller masses can be felt, freely movable, probably in omentum. Also enlarged glands in neck, more marked in axilla and groin, the largest the size of an English walnut. No tumor of bones or scalp. Lymph glands in groin same consistence as tumor; firm, somewhat elastic, no fluctuation. There is a puncture mark below umbilicus.

Skin pale. Muscles flabby. Rigor mortis present throughout. Panniculus very thin. Œdema marked over lower extremities.

Diaphragm at fourth intercostal space on right; fifth rib on left.

Mediastinum contains large numbers of enlarged lymph glands of somewhat firmer consistency than elsewhere.

Thymus: Large lymphoid masses in thymic fat; on section, uniform medullary consistency, very cellular.

Pleural cavities: Right contains about 1 liter grayish turbid fluid about same appearance as in peritoneal cavity, only thinner. Left, 300 c.c. same.

Pericardium: Sac not distended, fluid slightly increased, clear. Subpericardial fat increased.

Heart: Apex behind upper part of fifth rib, inside nipple line. Somewhat smaller than cadaver's right fist. Contains moderate amount of fluid blood and soft clots. Muscle rather pale, brown, soft; easily torn. Right heart: Auricle contains large antemortem white clots. Ventricle wall measures 2 to 5 mm., 1 to 2 mm. being fat. Left heart: Ventricle contracted. Wall measures 15 mm. Valves: Tricuspid orifice and valves negative. Pulmonary orifice and valves negative. Mitral flaps show nodular thickenings of proximal margin. Chordæ tendinæ thickened. Aortic semilunars show a slight thickening. Antemortem mixed clots extending into coronary artery.

Left lung: Old adhesions at base, free at apex. Slight thickening of pleura. Moderately distended. Moderate anthracosis. Hypostasis in lower lobe. Right lung: Completely collapsed;

cavity filled with grayish turbid exudate. Lung shows complete atelectasis, covered with dense fibrinous exudate. On section lung grayish. Small bronchi dilated.

Bronchi: Smaller ones dilated on left side, mucosa thickened; also on right contained purulent exudate. Bronchial glands: Greatly enlarged, œdematous on both sides; on section, soft medullary consistence; very cellular.

Aorta shows beginning arteriosclerosis.

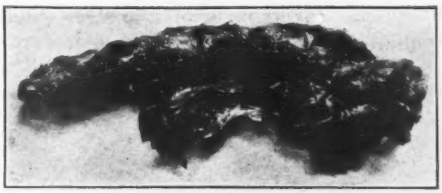


FIG. 1.—Upper part of the thoracic duct.

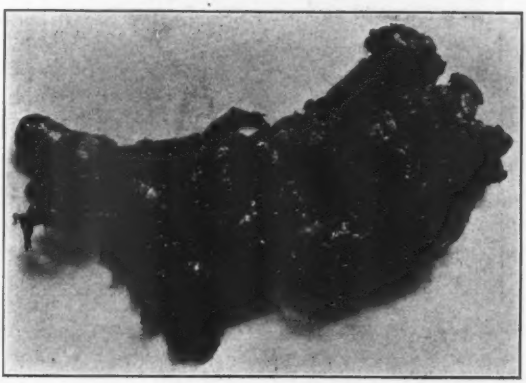


FIG. 2.—Lower part of the thoracic duct.

Thoracic duct: Extending from receptaculum chyli to subclavian is a solid cord of tissue, larger below, where it is about 4 to 6 cm. in diameter, gradually decreasing above to 2 cm., filling up the greatly dilated thoracic duct; on section it is pale, with scattered reddish spots, medullary, uniform consistence; very cellular, and resembling the abdominal tumor and the lymph glands in all respects. Above, this tumor mass projects slightly into subclavian. Below, the large mass in receptaculum chyli is directly connected with the retroperitoneal and mesenteric mass by cords of similar lymphoid tissue. (Figs. 1 and 2.)

Recent peritoneal adhesions around puncture wound. Omen-

tum is slightly rolled up below umbilicus, moderately rich in fat. Contains a number of enlarged lymph glands. On section, these resemble lymphoid masses elsewhere.

Spleen: About normal size, somewhat adherent to diaphragm by easily torn adhesions. Irregular in shape, upper part pale, partly separated from remaining portion on anterior margin by deep fissure running about five-sixths of the way across surface. Bottom of fissure covered by dense hyaline connective tissue, capsule thickened throughout, showing hyaline patches. On section, soft, pulp hyperplastic, covers up stroma to some extent. Follicles diminished in number, a few of larger size found.

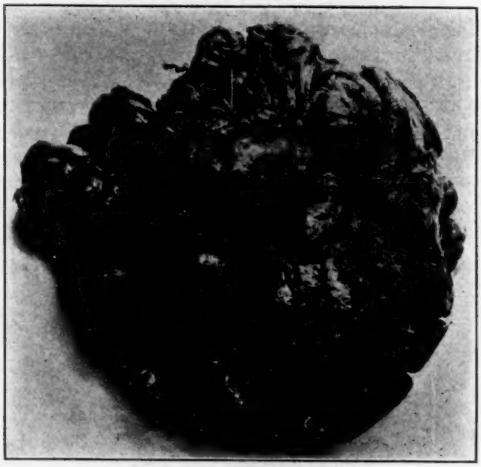


FIG. 3.—Mesenteric growth (with the intestines attached).

Arising from abdomen is a large nodular tumor mass occupying the position of the mesentery and the root of the mesentery (Fig. 3). Entire small intestine borders the lateral aspects of tumor. Smaller nodules and cords extend from main mass up on to intestine beneath serous coat. The mass measures 30 cm. transversely, 25 cm sagitally, 15 cm. anteroposteriorly. Larger part overhangs pelvis, is free, can be lifted up, but at the root of mesentery is continuous with a similar large nodular mass, occupying place of retroperitoneal glands. On section, the mass is found to be made up of nodules more or less confluent, presenting an appearance exactly like that in lymph glands, very cellular, yields abundant exudate, uniformly medullary, grayish white, spotted, and streaked with red.

Adrenals negative.

Left kidney 11×4×3 cm. Pelvis dilated. Mucous membrane

thickened. General appearance somewhat that of right. Over surface whitish nodules about size of pinhead. Right kidney 9×5×2.5 cm. Cortex, 4 to 6 mm. Fibrous capsule strips easily. Bleeds freely, rather uniformly dark-red color; otherwise negative. Outside fatty capsules of both large masses of lymphoid tissue, extending along bloodvessels.

Ureters both dilated, left more than right. Pushed somewhat to left by tumor mass on right side. Bladder moderately distended. Contains about 75 c.c. turbid urine.

Duodenum flattened by pressure of tumor. Wall atrophic; contains thin, yellow, bile-stained material. Common duct also compressed.

Stomach: Walls atrophic, postmortem change. Hypostatic congestion, with small hemorrhage. No enlargement of lymphoid tissue.

Liver 33×20×9 cm. Right lobe enlarged more than left. Capsule thickened around ligaments. Lower edge rounded, fairly firm. On section, moderately rich in blood. Periphery of lobules shows some fat. Consistency rather soft as a whole, central veins dilated. Numerous anemic areas. Lobules large. Islands of Glisson infiltrated.

Gall-bladder filled with thick bile, wall œdematous, serous surface thickened. Contains a number of facetted gallstones; central pigment and coating of cholesterin and lime.

Portal vein compressed by tumor.

Pancreas small, consistency soft.

Portal glands enlarged, same characteristics as elsewhere; vena cava compressed. Retroperitoneal glands enormously enlarged, forming a large nodular tumor, of the same character as that found in mesentery. Section shows soft medullary mass of almost homogeneous consistency, spotted with red. Scraping yields abundant cell juice. Mass extends from diaphragm to pelvis, 30 cm. long, 6 to 10 cm. thick. Prolongations continuous below the tumor masses along external iliac and femoral vessels, extending into pelvis along both sides of bladder.

External genitals markedly œdematous, especially scrotum and tunics of testicle. Body of right testis œdematous, otherwise negative. Left about size of right. Some thickening of epididymis. Prostate about normal size. On section, negative.

Sternum easily fractured; red narrow hyperplastic. Periosteum of sternum (under side) slightly thickened. Can be separated easily; leaves roughened bone surface. Lumbar vertebræ opened in body. Red marrow hyperplastic.

Microscopic findings. The abdominal tumor is made up of cells of lymphocyte type, fine delicate reticulum, no structure of lymph gland remaining, although each nodule appears to represent a lymph gland, remains of a capsule being found in many of them. The capsule is infiltrated with cells of the same type, this infiltration extending throughout fat and connective tissue of mesentery.

Cords of the same atypical lymphoid tissue extend through the lymphatics. The entire mesentery shows more or less infiltration of this character, the largest masses being found near the root. The wall of the small intestine is infiltrated, the infiltration varying in degree in different portions. The solitary follicles and Peyer's patches show similar tumor-like hyperplasia. Mucosa of stomach not involved. The lymphoid growths are very vascular, show numerous hemorrhages, and present very few small areas of degeneration and necrosis. A few mitoses are seen.

The retroperitoneal tumor has the same character as the mesenteric growths.

The mass in the thoracic duct is a lymphoid tumor of the same character as that in mesentery.

Peripheral lymph glands: All show a lymphoid hyperplasia with loss of characteristic lymph-gland structure, a uniform mass of lymphoid cells infiltrating capsules and tissue outside. The distinction between cortex and medullary portion is entirely lost, the sinuses are obliterated; there are no germinal centres. No giant cells or endothelial cells, a few eosinophiles.

Lung: Large lymphomatous nodules replace the peribronchial lymph nodes, and throughout the lung tissue there are nodules of varying sizes similar to that found in mesentery and elsewhere. The large, white, flattened areas of thickening on pleura are found on section to consist of subpleural lymphoid areas, corresponding to those found elsewhere.

Heart: Atrophy; fatty degeneration. No lymphoid areas or infiltration.

Spleen: Atrophy, congestion; the follicles are replaced by masses of lymphoid tissue, corresponding to that found elsewhere, but differing from normal Malpighian follicles.

Kidney: Cloudy swelling, atrophy, small areas of lymphoid infiltration into one kidney large enough to be seen with naked eye.

Liver: Marked periportal lymphoid infiltration, congestion, atrophy, some fatty infiltration.

Other organs: Show atrophy, congestion, some parenchymatous degeneration.

Bone-marrow: Lymphoid hyperplasia of bone-marrow.

So far the case seems not very different from one of multiple sarcoma, or malignant lymphoma or lymphosarcoma of writers, but the condition of the blood, when examined in detail, shows certain points of interest.

For microscopic examination of the blood cover-glass preparations were stained with Wright's stain and examined by counting continuously with a mechanical stage. The red cells show moderate variation in sizes. There are a few cells not more than 3 μ in diameter, a few slightly larger than normal, a few pear-shaped forms. A few very pale cells. No nucleated reds. The

leukocytes are chiefly mononuclear, the differential count being (652 cells): lymphocytes, 69.8 per cent.; large mononuclear and transition 0.7 per cent.; polynuclear, 27.4 per cent.; eosinophile, 1.3 per cent.; basophile, 3 per cent. The lymphocytes cannot easily be put into two groups of large and small. Normal small lymphocytes are few—about 1 per cent.—but there are variations in size from cells about the size of a red corpuscle up to cells twice that size, or, rarely, larger. Many have distinct, round but more or less fragmented nuclei, and a pale spongy or reticulated protoplasm in a ring or crescent about the nucleus. Others have paler, often thready or foamy nuclei, and in some no distinction can be made between nucleus and protoplasm, the cell taking the dye faintly, in a fine network, though with its outline is well preserved. There are also cells with notched, incised, reniform, or saddle-bag nuclei, having the general characters of the others in this group. In other words, the lymphocytes show distinct leukemic features. The cells called large mononuclear are few, with large bodies, pale nuclei, round, oval or irregular and very pale protoplasm. The polynuclears show considerable variation in size, up to twice the normal, with nuclei usually large in proportion. There are no very small ones. Their granules stain well and they show only slight tendency to complete separation of the parts of the nuclei. The eosinophile cells are all polymorphonuclear, and of normal size. The mast cells are of medium size, with polymorphonuclei.

I have counted only well-preserved cells. There are many degenerates—45 to 50 of all others. They are all, apparently, of lymphocyte origin and are easily distinguished from the others. Even without these it is obvious the blood is lymphocythemic, though the total number of cells, even with degenerates, is not much increased.

The sediment of the ascitic and pleural fluids shows lymphocytes almost exclusively. There are in both a few larger cells, of endothelial origin, but so few, and so irregularly scattered, that a comparative count could only be made by including many thousands of all cells. The lymphocytes in these fluids show the same characteristics as those in the blood. The endothelial cells are small, as a rule, have few vacuoles or other degenerative features, have deeply-staining nuclei and rather slightly basophile protoplasm.

A CONTRIBUTION TO THE STUDY OF LONG-CONTINUED FEVERS.[1]

By Herbert C. Moffitt, M.D.,
PROFESSOR OF THE THEORY AND PRACTICE OF MEDICINE IN THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, CALIFORNIA.

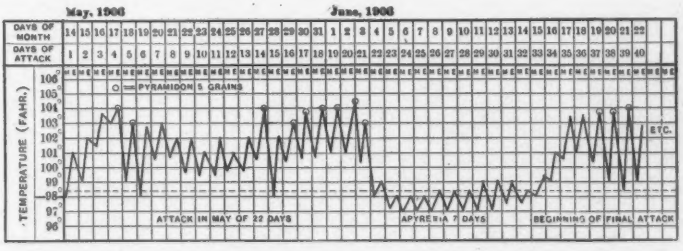
Through the kindness of Dr. F. H. Humphris, of Honolulu, there was referred to me in July, 1906, a lady of forty-seven years with the following interesting history: There had been no tuberculosis or malignant disease in the family. She had been twice married—the first time at sixteen—and had one child living and well. As a girl, she was said to have had malaria. In 1893 she had been infected with syphilis, which was treated three months at Arkansas Hot Springs, and again for some weeks in 1900. For ten years there had been a cough each winter lasting three or four months, annoying rather than serious, and only occasionally keeping her in bed. During these years there had been four or five attacks of so-called "la grippe," attended with fever for a few days, cough, and aching. In 1895 a curettage was done for some slight uterine derangement, but there had never been serious pelvic symptoms. In 1898 an acute attack of abdominal pain was referred to the appendix, and Dr. Murphy, of Chicago, operated later in the year and removed an appendix showing slight pathological changes.

During 1902 and the first half of 1903 she was very well and travelled extensively. In the latter part of 1903 and the first months of 1904 she had three attacks of sudden, severe abdominal pain. The pain was general throughout the abdomen, colicky, lasted a few hours, and was thought due to eating fruit and drinking mineral water. In Paris, during the summer of 1904, she was tired, nervous, and had little appetite, but felt well during the autumn in St. Louis. A little later, in Chicago, there was fever for a few days, with headache and aching in the muscles, and she felt badly for a month. The usual bronchitis kept her rather miserable during the winter of 1904 and 1905 in Paris, and an attack called "la grippe" confined her to the house for a few days in March. In the summer months, in New York, she felt tired, had very little appetite, and was said to have liver trouble. She was much better a little later in Canada and the Northwest, and felt perfectly well when she sailed for Honolulu in September, 1905. The patient had always been a great traveller. She spent 1902 in France, Italy, and Austria. In 1903 she was in Japan, Honolulu, Mexico, France, and Spain; in 1904 in Italy, the Riviera, Greece, Turkey, the Mediterranean and Egypt.

[1] Read at a meeting of the Association of American Physicians, Washington, D. C., May 7, 8, and 9, 1907.

The present illness began on the steamer two days before reaching Honolulu, in September, 1905. There was intense muscular soreness, considerable pain in the joints, and fever lasting a week. She was then perfectly well for two weeks until pain and fever recurred on the trip to Australia. This attack lasted a week, and was followed by an apparent complete recovery. After two weeks, however, she had recurrence of the familiar prostration and fever and was under the care of Dr. Hooper, of Melbourne, for a time. A blood examination, made October 24, 1905, by Dr. F. W. Wilkinson, showed red corpuscles, 4,600,000; white corpuscles, 8000; hemoglobin, 90 per cent.; no malarial parasites; a distinct increase of large mononuclear leukocytes.

After this attack she felt well, and was able to travel considerably about Australia. From October to February there were three similar periods of pyrexia, but she was not confined to bed. In February there was a severe attack in Rotorua lasting a week, during which joint and muscle pains were intense. Since that time there has been absolutely no pain, and recurrent pyrexia has been the sole feature (see the accompanying chart).



The course of the disease to August 28, 1906, when the patient died, is given in the subjoined table.

No. of attack.	Pyrexia.	Apyretic interval. (Approximate.)
1	7 days	14 days
2	7 "	14 "
3	10 "	not known
4	7 "	" "
5	7 "	" "
6	7 "	" "
7	7 "	10 days
8	7 "	10 "
9	3 "	14 "
10	7 "	14 "
11	22 "	14 "
12	22 "	9 "
13	75 "	

During the first attacks aching in the muscles and joints was intense, and suggested dengue. In the intervals health was perfect,

and the patient travelled, ate well, and nothing suggested a return of the trouble until fever recurred. The temperature rose rapidly, but not abruptly, and fell by lysis; during the intervals, when measured, it was slightly subnormal. With the recurrence of temperature, there was increased constipation, some bloating, malaise, and, in the later periods, great prostration, occasional chills, and great discomfort from sweating. Under Dr. Humphris' observation, the pulse was of good quality, from 74 to 90; quinine did not affect the temperature, and made the nervous symptoms worse; pyramidon, in 5-grain doses, was found to give much relief, with a quick drop in temperature and profuse sweating. Until July there was no evidence of cachexia, and the absence of symptoms and signs was in striking contrast to the monotonous daily temperature.

When seen July 20, the patient had a peculiar earthy color, not unlike that seen in liver abscess. There was fever of a marked remittent, intermittent type. Shaking chills occurred every three or four days. At the height of temperature, there was great restlessness, sometimes mild delirium, but no pain. Pyramidon was occasionally required to control temperature; 5 grains would be quickly followed by a drop of 3° to 5° and a drenching sweat. Even without pyramidon, profuse sweating was frequent.

There were slight changes at both apices, but no evidence of an active process. The chief thing of interest in the thorax examination was the curved line of liver dulness, reaching to the fourth rib in the mammillary and anterior axillary lines, to the angle of the scapula and down to the eleventh spine at the vertebral column. Despite the enlargement of the liver upward, which showed beautifully on an *x*-ray plate, there was at no time any evidence of enlargement downward. The area of splenic dulness was frequently a little large, but the spleen was never palpated in almost daily examinations over a period of four weeks. The heart was markedly dilated, particularly the left ventricle, and there was a systolic murmur over the precordium, with greatest intensity over the base. The pulse was slow in comparison to the temperature, averaging 80 to 100.

The abdomen was considerably distended, not tender, and in the last days a small amount of free fluid could be demonstrated. Superficial glands could never be palpated, nor were there glands to be felt in the abdomen or by rectum. The follicles of the tonsils and base of the tongue were not enlarged—in fact the tongue suggested the smooth atrophy of Virchow, but was not positive. There was extreme myosis, which had been noted for some years. The pupillary outline was irregular, and reaction to light was practically absent. There were no fundus changes, and nothing else in the nervous system to suggest syphilis. Pelvic and rectal examination was negative. The urine at different times showed a trace of albumin, and a few hyalin casts. Diazo reaction was constantly present,

sometimes faint, and again well marked. In the last days urobilin was present in considerable amount, with a trace of bile. The stools were microscopically negative, and contained no occult blood.

Cultures in bouillon, made on two occasions, with blood from puncture of a vein gave no growths. Serum reactions with cultures of typhoid and paratyphoid bacilli, and Micrococcus melitensis were negative in dilutions of 1 to 50 and 1 to 20. Of principal interest in the blood counts (see the accompanying chart) was the moderate secondary anemia, with marked leukopenia and relative increase in the large mononuclear forms. Some of these cells were distinctly larger than the normal type.

Date.	Reds.	Whites.	Percentage.					Remarks.
			Polynuclear	Small mononuclear	Large mononuclear	Eosinophiles.	Hb.	
October 24, 1905	4,600,000	8000	.....	.....	Increase.	.....	90	No plasmodia. Made by Dr. John F. Wilkinson, Melbourne.
May 2, 1906	5,800,000	7200	78.0	21.0	1.0	.....	...	No plasmodia. Made by Dr. Humphris, Honolulu, T. H.
May 21, 1906	5,600,000	5800	67.0	32.0	.....	1.0		
July 21, 1906	4,416,000	3000	83.0	8.0	9.0	.....	70	Temperature 102°. Slight variation in size of red cells.
July 24, 1906	.....	5500	72 5	12.0	15.5	.....	...	After chill. Temperature 104°.
July 28, 1906	4,032,000	2800	65.0	15.5	19.5	.....	...	No plasmodia. Few degenerated reds.
August 4, 1906	3,100,000	5200	73.0	9.0	18.0	.....	70	5 P.M., after chill. Temperature 103.6°.
August 11, 1906	3,272,000	2600	80.0	9.0	11.0	.....	60	No nucleated reds.

With the peculiar recurrent pyrexia, the conditions considered in diagnosis were chiefly Malta fever, Hodgkin's disease or lymphosarcoma, syphilis of the liver, and gallstones in the common or hepatic ducts with catarrhal cholangitis. The aching of joints and muscles in the early periods, the undulant fever, the recent visit to many Mediterranean ports would suggest Malta fever, but the frequent repetition of attacks and the negative serum reaction decided against it. Serum reactions in this disease are not always unequivocal.[2]

Echinococcus of the liver was suggested by the shape of the right

[2] An army pathologist of wide experience sent a man to the hospital with the diagnosis of Malta fever from the agglutination test; but the recurrent fever later cleared up on drainage of an unrecognised empyema. In another case with positive serum reaction, gonorrheal infection was shown to be the cause of temperature and of joint symptoms.

lobe, but the radiogram gave no characteristic picture, and the absence of eosinophilia and leukocytosis spoke against it.

The absence of jaundice was much against a ball-valve calculus in the common duct. The occasional complaint of distress over the liver, with a feeling of distention in the abdomen, suggested the possibility of a calculus in the hepatic ducts, as in the cases of Frerich[3] and Schmitz.[4] The failure of a polynuclear leukocytosis just after a chill and rapid rise of temperature, was decidedly against an infective cholangitis. My experience has been that of Pick,[5] that in cases of infective cholangitis (of pyelitis and nearly all cases of malignant endocarditis as well), there is a decided polynuclear leukocytosis just after a paroxysm of chill and fever. There may have been a normal count, or a leukopenia, with normal ratio, during the febrile or afebrile period before the paroxysm, and the sudden change in the blood picture is most striking.

Despite the characteristic alternating pyrexia, the absence of palpable glands and spleen, and of enlarged mediastinal glands, was much against Hodgkin's disease or lymphosarcoma limited to the liver; although the cases of Naunyn[6] and Rolleston[7] had lately been brought to my mind in reviewing a case of intermittent hepatic fever.[8]

Naunyn mentions the case of a woman of forty with intermittent fever for some months and paroxysms of chill, fever, and sweating recurring about 4 P.M. daily. There was considerable liver enlargement and an irregular tumor of the left kidney. The patient demanded operation on account of the unsupportable chills and sweating. The left kidney was removed, and contained a sarcomatous mass the size of an apple. The liver appeared normal. The chills and fever ceased, and the patient improved until, after four weeks, the fever recurred. Death occurred from exhaustion, and at autopsy metastases were found in retroperitoneal and medistinal glands, and a large central mass in the liver.

The history of syphilis, the pupillary changes, the signs of some liver affection, demanded specific therapy. Mercury was given by inunctions and hypodermically, and iodide was administered up to 6 grams daily in combination with ascending doses of Fowler's solution. There was no improvement at the end of three weeks; the

[3] Leberkrankheiten, Band ii, 495.

[4] Berl. klin. Woch., 1891, 915.

[5] Zur Diagnostik der Infekte der Gallenwege, Mittheil. aus den Grenz., d. Med. u. Chir., viii, 174; Ueber Intermittirendes Gallenfieber, Deut. Arch. f. klin. Med., lxix, 1.

[6] Cholelithiasis, S. 69.

[7] Diseases of the Liver, p. 388; Ibid. p. 152.

[8] Rolleston in writing of lymphosarcoma of the liver records that: "Exceptionally the organ is very considerably enlarged, and if the superficial lymphatic glands available for clinical examination are but little affected, the clinical aspect of the case, especially when there is a hectic temperature, may suggest hepatic abscess, as in a case under my care." Again, "Some years ago a man was under my care with a pedunculated mass in the left groin of many years' standing, which turned out to be lymphadenoma; he developed a hectic temperature and considerable enlargement of the liver. The condition was not unlike hepatic abscess, and the question of operation was raised during life."

patient was weaker, slight icterus developed, and moderate ascites could be demonstrated. Operation was demandad by the patient for relief of the intolerable discomfort caused by the temperature and sweating, and an exploratory laparotomy was done by Dr. Beverly MacMonagle in the hope of finding an abscess, or, as in Israel's case, a gumma that could be reached surgically. On opening the abdomen a moderate amount of blood-stained fluid escaped. The liver edge was a little above the costal margin, was irregular, rounded, and the liver was studded with whitish, irregular nodules the size of a pea or a small marble. A piece of the liver was removed and sent to Dr. William Ophüls for examination. The wound was closed, and the patient sent to bed in fair condition, but death occurred next day from exhaustion.

The following is Dr. Ophül's report: "Sections show multiple tumor nodules, which, in the periphery, consist almost entirely of very large round or oval cells. Many of these cells show mitotic figures. The central parts of the nodules are made up of somewhat smaller cells, with some connective-tissue fibers between them. No caseation. In the periphery the tumor infiltrates the liver tissue following the course of the lymphatics along the capillaries. No definite alveolar arrangement can be made out in any place. The tumor has the appearance of a sarcoma."

At the autopsy the lungs were found emphysematous, with puckered scars and shrinking at both apices. The heart was flabby, much dilated, the endocardium normal, the ascending aorta dotted with atheromatous patches. Near the hilum of the right kidney, which was in normal position, was a large retroperitoneal gland the size of a golf ball. This was the only gland enlarged anywhere in the body, except a few pigmented glands the size of small beans, such as one usually sees about the roots of the lungs. The follicles of the gastro-intestinal tract were not enlarged. Chiefly remarkable was the enlargement of the dome of the liver, as had been determined clinically; the diaphragm was pushed up to the third rib. The failure of the liver to enlarge downward was explained by the puckering of the rounded edges by several deep scars and the presence of several firm adhesions to the anterior abdominal wall—plainly the result of an old luetic process. Great numbers of whitish nodules studded the right lobe of the liver; there were only five or six in the left lobe. The spleen was not enlarged, 12 by 7 cm.; on section there were three whitish, irregular nodules the size of lima beans similar to the growths in the liver. Microscopically the tumors of the lymph gland, liver, and spleen showed a similar structure to the nodule removed at operation. There was no caseation. Giant cells and eosinophiles were not present. No tubercle bacilli were found in the smears from the gland tumor. The growth would be best classed, therefore, as a lymphosarcoma.

Retrospectively, it would seem that the attacks of abdominal pain

in 1904 marked the beginning of the disease, probably in the retroperitoneal gland, and that the fever, general pains, and indefinite symptoms in the hepatic region of the last year signalled the invasion of the liver. It is difficult to assign a definite role in etiology to syphilis, nor can the limitation of the malignant process to one lymph gland be in any way explained. Syphilis may perhaps have rendered the liver less resistant to invasion of the growth. Treatment would probably have availed little at any stage of the disease. Large doses of arsenic and specific treatment were given during the last month of life without effect. *X*-ray treatment and Coley's serum might have been tried in the apyretic intervals. *X*-ray treatment was out of the question while the patient was under my care, owing to the pyrexia and cachexia; it is, even in afebrile cases, at times distinctly detrimental.[9]

Recurrent fever in tuberculous lymphomas, in Hodgkin's disease, in lymphosarcoma or sarcoma of other varieties has been chronicled in numerous papers: Dr. Musser reviewed the literature, and added two personal cases in a communication to this Association in 1901. Graves mentioned occurrence of the peculiar temperature in some cases of lymphomas before Murchison's[10] paper in 1870. Gowers[11] introduced the name alternating pyrexia in his article on Hodgkin's disease in Reynold's *Practice*; Southey (1875) and Sainsbury were among the early English authors recording cases; Pel[12] in 1885, and Ebstein[13], in 1887, called general attention to the peculiar fever type, and Ebstein thought he was describing a new clinical entity, which he termed "das chronische Rückfallsfieber." It soon became recognized, however, that recurrent fever is a symptom and not a disease. The papers of Graves, Murchison, Southey, Gowers, Sainsbury, Pel, and Ebstein dealt with Hodgkin's disease. In Klein's[14] case, reported as cirrhosis of the liver and pseudoleukemia with recurrent fever, the history suggests strongly that fever was of the intermittent hepatic variety. Two of Kast's[15] cases would be classed clinically as Hodgkin's. In a boy of seven, with enlarged glands, spleen, and liver, there were nine periods of pyrexia, and toward the last a leukocytosis (the kind not described)

[9] In an old man with generalized Hodgkin's disease, who had previously had periods of pyrexia, a few *x*-ray exposures were followed by remittent fever, which persisted till death some three weeks later. A man aged forty years had recurrence of lymphosarcoma in the spleen and liver six months after a primary tumor in the glands of the right axilla was removed. Four attempts were made at *x*-ray treatment. Each time, after three or four short exposures over the liver and spleen, there would be a chill followed by rapid rise of temperature to 103° or 104°, prostration, loss of appetite, and persistence of fever for four or five days.

[10] Trans. Path. Soc. Lond., 1870, xxi, 372.

[11] Reynolds' System of Medicine, 1879.

[12] Zur Symptomatologie der sogenannten Pseudoleukæmie. Berl. klin. Woch., 1885, 3; Pseudoleukæmie oder chronisches Rückfallsfieber. Berl. klin. Woch., 1887, 644.

[13] Das chronische Rückfallsfieber. Berl. klin. Woch., 1887, 565.

[14] Ein Fall von Pseudoleukemie nebst Lebercirrhose mit recurrierendem Fieberverlauf. Berl. klin. Woch., 1890, 712.

[15] Ueber Rückfallsfieber bei multipler Sarkombildung.

of 100,000, and later, 270,000. Grawitz mentioned a case with enlarged glands becoming softer during the attacks of fever, negative blood cultures, and no bacteria in the glands at autopsy. Janz[16] extirpated the spleen in a case reported as pseudoleukemia; streptococci were found in many glands and tubercle bacilli in one supraclavicular gland. Fischer,[17] reporting 12 cases of Hodgkin's disease, in which cultures from the blood and glands were negative, mentioned one instance with periodic fever in which organisms were found in the blood during the pyrexia, but not in the intervals. Laache[18] saw Hodgkin's disease with alternating pyrexia, and noted decrease in size of the glands during the fever and increase in the apyretic intervals. He mentions that Fiedler reported recovery in a case of Hodgkin's with recurrent fever. The communications of Van der Scheer,[19] Barbrock,[20] Kissel,[21] Westphal, Verdelli,[22] Freudweiler,[23] likewise deal with Hodgkin's disease or "pseudoleukemia," as do recent artcles by Hirschfelder[24] and Clarke, Stoll,[25] Ruffin,[26] and Tschistowitsch.[27]

Shortly after Ebstein's paper it was shown that "chronisches Rückfallsfieber" might occur as a striking symptom of malignant disease. Renvers[28] reported lymphosarcoma of the retroperitoneal glands, liver, and spleen, marked clinically by recurrent pyrexia in seven periods of seven days each. In Voelcker's[29] case, with typical undulant fever, there was a sarcoma of the lumbar spine and retroperitoneal glands. Hanser[30] reported ten cycles of fever with an epigastric tumor regarded as sarcoma. In Hewelke's[31] case of retroperitoneal lymphosarcoma, staphylococci were found four times in blood cultures taken during both febrile and afebrile stages. Multiple myelomas were found as the cause of fever recurring at

[16] Zur Operation der leukemischen Mils. Beitr. z. klin. Chir., 1899, xxiii, 287.

[17] Ueber malignes Lymphom. Arch. f. klin. Chir., 1897, lv, 467.

[18] Ebstein und Schwalbe's Handbuch, i, S. 844.

[19] Een geval van pseudoleukemie med gedeeltelyk recurrend Koorstype. Neederl. Weekblatt, 1899.

[20] Ueber Pseudoleukemie mit intercurriendem Fieberverlauf. Virchow und Hirsch's Jahresberichte, 1890, ii, 331.

[21] Maligne Neubildungen und chronisches Rückfallsfieber, Vratsch., 1895, No. 35; Drei Faelle von Hodgkinischer Krankheit bei Kindern Vratsch, 1895, 651.

[22] Archivo italiano di clinica medica, 1895.

[23] Statistische Untersuchungen über Fiebererscheinungen bei Carcinom innerer Organe. Deut. Arch. f. klin. Med., lxiv, 544.

[24] A Case of Hodgkin's Disease with Chronic Recurrent Fever. Occidental Med. Jour., 1904, xviii, 11.

[25] A Case of Hodgkin's Disease with Slight Enlargement of Peripheral Glands. Med. Record, 1905, p. 773.

[26] Hodgkin's Disease. A Study of a Case with Relapsing Fever. Amer. Jour. Med. Sci., 1906, p. 587.

[27] Ueber Pseudoleukemie mit periodischen Fieber. Deut. med. Woch., 1907, 502.

[28] Ueber Lymphosarkomatose mit recurriendem Fieberverlauf. Deut. med. Woch., 1888, 753.

[29] Ueber Sarkom mit recurriendem Fieberverlauf. Berl. klin. Woch., 1889, 796.

[30] Ein Fall von chronischem Rückfallsfieber. Berl. klin. Woch., 1889, 692.

[31] Lymphomatosis retroperitonealis maligna cum febre recurrente Kronika lekarska, 1889, xii.

intervals of one to twelve days over a period of nine months in a case recorded by Hammer.[32] Subohn[33] reported a questionable instance of recurrent fever with lymphosarcoma of the thymus, and Witthauer[34] noted periodic fever through five months in a round-cell sarcoma of the posterior mediastinum. Kast, beside the 2 cases mentioned above, described recurrent fever in a sarcoma of the hip and retroperitoneal glands occurring in a boy of sixteen. The papers of Puritz,[35] Bulubasch,[36] Kissel, Glaeser,[37] Hohenemser, deal also with the association of alternating pyrexia and sarcoma. Hampeln,[38] Anker,[39] Kobler,[40] Kast and Freundweiler write of its occurrence with carcinoma.

Delafield[41], and a little later Askanazy[42], first called general attention to the similarity of many cases of tuberculosis of the lymphatic system and Hodgkin's disease. Musser's[43] 2 cases of recurrent fever were tuberculous. In No. 8 of Sternberg's[44] series, this type of fever was noted, but the cases should be classed as Hodgkin's disease with terminal tuberculous infection. Schur[45] reported a combination of Hodgkin's disease and tuberculosis, with alternating pyrexia and a polynuclear leukocytosis of 30,000. Crowder described a case of generalized tuberculosis with irregular fever, a leukocytosis of 19,000, and the clinical picture of Hodgkin's disease; tubercle bacilli and staphylococci were found in the glands at autopsy. Strauss[46] saw a female patient with enlarged cervical glands and chronic recurrent fever. At one time there was such a marked lymphocytosis as to suggest lymphatic leukemia, but tuberculous glands were found at operation.

[32] Primäre sarkomatöse Ostitis mit chronischem Rückfallsfieber. Virchow Arch., 1894, 137, 280.

[33] Jahrbuch der Hamburger Staatskrankenanstalten Leipzig, 1892, 65.

[34] Intermittirendes Fieber als Symptom eines Mediastinaltumors. Münch med. Woch., 1901, 224.

[35] Ueber Sarkom mit sogenanntem chronischem Rückfallsfieber. Virch. Arch., Band 126, 1312.

[36] Sarkom der inneren Lymphdrüsen mit febris recurrens. Medicinskoe obroseme, 1894, Band 40–41, 601.

[37] Mit recurriendem Fieber verlaufende multiple Sarkomatose. Med. allg. Centralzeitung, 1897, 601.

[38] Zur Symptomatologie occulter visceraler Carcinome. Zeit. f. klin. Med., viii, 221; Ueber intermittirendes Fieber im Verlauf des Magencarcinoms. Zeit. f. klin. Med., Band xiv, 566.

[39] Ueber das Vorkommen intermittirendes Fieber bei chronischen Krankheiten. Inaug. Diss. Strassburg, 1890.

[40] Ueber typisches Fieber bei malignen Neubildungen des Unterleibs. Wien. klin. Woch., 1892, No. 23, 335; No. 24, 352.

[41] A Case of Acute and Fatal Tuberculosis of the Lymphatic Glands. Med. Record, 1887.

[42] Tuberculöse Lymphome unter dem Bilde febriler Pseudoleukemie verlaufend. Ziegler's Beit., 1888, iii, 413.

[43] Note on the Fever of Hodgkin's Disease. Amer. Med., 1902, iii, 13.

[44] Ueber eine eigenartige unter dem Bilde der Pseudoleukemie verlaufende Tuberculose des lymphatischen Apparats. Zeit. f. Heilkunde, xix, 21.

[45] Zur Symptomatologie der unter dem Bilde der Pseudoleukemie verlaufenden Lymphdruesentuberkulose. Wien. klin. Woch., 1902.

[46] Sarcomatose und lymphatische Leukemie. Char. Annalen, xxiii, 343.

Although resting on diff rent pathological bases, the clinical features of all these cases are strik ngly similar. Febrile periods of from three to seven or ten days alternate with afebrile intervals of the same or slightly longer duration. As the disease progresses, the febrile periods usually lengthen, and continued fever of a remi tent type may be present for weeks or months. The last attack in the case here reported was of seventy-six days' duration. The temperature usually rises and falls slowly, but there may be an abrupt rise with or without chill. Sweating is not uncommon. In the intervals between the first few febrile attacks the patients may feel and look perfectly well, but weakness, anemia, and cachexia gradually appear. Fever is frequently the fisrt symptom. The onset may be sudden, as in one of Pel's cases. Pain in the abdomen, as an early symptom, was noted by Ebstein, Hanser, and Voelckers. It occurred in three distinct attacks in the case here described. In Hammer's case of multiple myelomas, pain in the chest was the first symptom. A patient of Musser had severe pain in the right inguinal region with each pyrexial attack.

Pel, Ebstein, Bulubasch, Klein, and Tschistowitsch described yellowish discoloration of the skin with patchy, brownish pigmentation. Terminal icterus was noted by Pel, Ebstein, Musser, and Klein. Enlargment of the peripheral glands was absent in not a few cases (Pel, Ebstein, Renvers, Barbrock, Voelckers, Hanser, Tschistowitsch). The retroperitoneal and bronchial glands are more frequently involved. Absence of splenic tumor is not recorded in any case, except the one here noted. Spleen, liver, and palpable glands nearly always increase in size during the periods of fever, and frequently become tender. Laache noted a swelling of the glands in the afebrile periods and decrease of size with pyrexia.

The urine showed no characteristic changes. Albumin was infrequent, urobilin and bile pigment were occasionally noted. Diazo reaction was noted by Renvers, Stoll, and in my case. Examination of the blood helps in the diagnosis chiefly by ruling out other causes of fever. Secondary anemia becomes marked as the disease progresses. Stoll recorded a count of 1,700,000 red cells and 30 per cent. hemoglobin. Leukopenia is more common than leukocytosis. Polynuclear leukocytosis would speak more for tuberculous lymphomas than for Hodgkin's disease or lymphosarcoma. Strauss, however, noted a marked lymphocytosis in a tuberculous case, and a leukocytosis of 270,000 was recorded by Kast in a boy of seven. Relative increase of the large mononuclear cells has been described in several instances. It must be remembered, in differentiating from septic affections, that positive blood cultures have occasionally been reported. Positive or suggestive evidence of syphilis was found by Pel, Klein, Renvers, Voelckers, Tschistowitsch and myself. In 27 instances in which sex was recorded, there were 16 males and 11 females. Recorded ages

varied from six to fifty-nine years. It is interesting to note that a number of patients had travelled extensively in the tropics. Recovery was noted in but 2 cases. Laache mentions a report by Fiedler, and Tschistowitsch observed prompt cure under iodide after many other drugs had been tried for months. Death has occurred in all other cases, usually from exhaustion.

Recurrent attacks of fever may occur over long periods of time in many other conditions, and differential diagnosis is by no means always easy. Repeated relapses in typhoid fever will not often give difficulty; blood cultures will help in the cases in which Widal reaction is absent or long delayed. Claisse[47] has lately written on typhoid fever with numerous relapses. In my opinion, great hesitation should attend the diagnosis of sporadic cases of Malta fever. Piroplasmosis should be considered in all cases of continued fever from the tropics, and examinations made from splenic punctures if necessary.

Hampeln was the first strongly to emphasize the occurrence of fever in carcinoma. The papers of Kraussold and Max Freudweiler are more recent. Fever may be an early symptom; in a case of Hampeln there was fever for three months before a diagnosis was made. Continued fever is rare, and the remittent, intermittent, or hectic type the most common. Periodic attacks may be noted and ague-like paroxysms of chills, fever, and sweating. In 475 cases of carcinoma collected by Freudweiler temperature over 38° C. was present in 24.6 per cent. The carcinoma may cause fever even without ulceration: in 14 out of 64 cases reported by Freudweiler there was no ulceration.

Heubner[48] mentions fever recurring in eight periods during the fall and winter in a child of four. At first there were only general symptoms during the febrile attacks, but later pus appeared in the urine, and the diagnosis of pyelitis was assured. The frequency of pyelitis both in children and adults needs constant emphasis. It must be remembered also that renal calculi may rarely give rise to recurrent paroxysms of chills, fever, and sweating without any urinary signs; the attacks are similar to those of intermittent hepatic fever. The attacks may occur, first, in tuberculous pyelitis; second, in calculous pyelitis; and, third, in rare instances of stone in the pelvis, without chronic suppurative pyelitis." (Osler.)[49]

[47] Fievre typhoide prolongie avec rechutes multiples. Bull. et. mem. Soc. med. des Hop. de Paris, 1906, xxiii, p. 571–574.

[48] Ueber langdauernde Fieberzustende unlkaren Ursprungs. Deut. Arch. f. klin. Med., lxiv, 35.

[49] On Fever of Hepatic Origin, Particularly the Intermittent Pyrexia Associated with Gallstones. Johns Hopkins Hosp. Reports, vol. ii, p. 1.

Some years ago a woman aged forty-five years was under observation for recurrent fever of a years' duration. With periodic temperature, there would be occasional chills and

Romberg[50] mentions 2 cases with anemia, enlargement of the spleen and liver, and fever of months' duration—in 1 case of continued type; in the other with apyrexial intervals of weeks' duration. A mitral murmur was interpreted as of functional origin, and both cases went to autopsy with a diagnosis of Hodgkin's disease. The postmortem revealed malignant endocarditis. Fever and progressive weakness and anemia may be the only symptoms of infective endocarditis. There may be apyretic intervals of days and weeks at a time. The interpretation of heart murmurs in cases with high temperature and anemia is, as Bloch[51] has pointed out, often peculiarly difficult. Infective endocarditis grafted upon an old valvular lesion may run an extremely chronic course, over a year (Dreschfeld), thirteen months (Osler), and fifteen months (Romberg). Cases under my observartion with autopsy verification have lasted six, fifteen, and eighteen months. With absence of signs of heart involvement, diagnosis of the condition may be difficult or impossible. Cases of this kind have recently been reported by Cole[52] and Bramwell.[53] In chronic cases, leukocytosis may not occur; repeated counts in a case lasting fifteen months showed a leukopenia of 3000 to 5000, with a relative lymphocytosis. Ewing[54] holds that "leukocytosis is present probably in all cases, but is often intermittent, and single observations may fail to discover it." There is frequently a decided increase in the polynuclear count after a chill, and abrupt rise of temperature. Blood cultures are of great help in diagnosis.

Frequent mention has been made of intermittent hepatic fever. Pain in the region of the liver and jaundice deepening after paroxysms of chill and fever usually make diagnosis reasonably certain. In a case seen some years ago there was no jaundice until eight months after fever was noted. The increase of leukocytes, after chill and fever, as described by Pick has been twice observed. Pain and jaundice may be absent, and the temperature curve the only characteristic feature. Frerichs has described long-continued intermittent fever with stone in the hepatic duct, and Schmitz reported 2 cases of recurrent attacks of intermittent

sweats, and complaint of dull aching in the right hypochondrium and lumbar regions. Leukocytes were normal in apyretic intervals, but after a chill and abrupt rise of temperature, there was several times noted a polynuclear leukocytosis of 28,000 to 36,000. There was a history of hematuria some years before, but the urine never contained albumin, blood or more than a few leukocytes. Operation revealed a large stone in the pelvis of the right kidney with a catarrhal pyelitis, no complete blocking of the ureter and no pyelonephritis. The fever with intermittent pyonephrosis (especially in tabetics) is, in my experience, frequently misinterpreted.

[50] Krankheiten der Kreislaufsorgane. Ebstein und Schwalbe, Handbuch der Praktischen Medizin, i, 685.

[51] Ueber Blutkrankheiten unter dem Bilde der akuten Endocarditis. Deut. med. Woch., 1903, 512.

[52] Johns Hopkins Hosp. Bull., xiii, p. 252.

[53] Clin. Studies, Edin., 1905–1906, n.s. iv, p. 193–207.

[54] Clinical Pathology of the Blood, p. 360.

pyrexia without pain or jaundice, in which cessation of fever followed passage of gallstones.

Many interesting papers of late have dealt with fever in visceral syphilis. Janeway[55] presented a communication on "Fever in Tertiary Syphilis" to this society in 1898. Riedel[56] cites remarkable cases in his article "Ueber die fieberhaft veraufende Lues der Gallenblase, Gallengänge, sowie der Leber," and quotes "den alten Satz, dass man bei unklaren fieberhaften Krankheiten immer zuerst an Tuberculose, so dann an Lues, endlich an Aktinomykose denken soll." F. Kemperer[57] reports several cases of syphilis of the liver with fever; in 1 case there was alternation of pyrexia with afebrile intervals over a period of a year. Recent literature on the subject is given in the articles of Klemperer and Raubitschek.[58]

In the past year Gilman Thompson called attention to the similarity between some cases of exophthalmic goitre and infective endocarditis. Two years ago an army captain was under my observation for some months. The chief complaint was of weakness, irritability, with occasional attacks of diarrhœa, chills, fever, and sweating. There was cachexia, a mitral systolic murmur, a pulse of 120 to 140, and irregular temperature recurring at intervals of days or weeks. The case was regarded as one of malignant endocarditis, until tremor, the general nervous picture, and Graefe and Stellweg signs decided for Parry's disease, even with absence of exophthalmos and goitre. A goitre developed later, and an operation by Dr. Halsted led to great improvement.

It is not uncommon to see children or young adults with long-continued or, more rarely, recurrent pyrexia, dependent upon tuberculosis of mediastinal, mesenteric, or retroperitoneal glands. A boy of eight was seen a year ago who had had moderate fever almost daily for six months. There was a history of pertussis one year before and examination showed enlarged bronchial glands. A young woman, seen four years since, had, as chief complaint, pain in the lumbar spine and in both loins. There was recurrent pyrexia of moderate degree over a period of eight months without satisfactory explanation. A radiogram showed the spine normal, but gave the shadows of several calcified retroperitoneal glands.

In a remarkable case, seen three years ago, a young woman of tuberculous family, had had recurrent pyrexia for over twelve years. Fever recurred two or three times in one year, and again not for two or three years. There were no symptoms during the attacks beyond prostration and temperature of 103°

[55] Fever in Tertiary Syphilis. Trans. Assoc. Amer. Phys., 1898.

[56] Ueber die fieberhaft verlaufende Lues der Gallenblasse, Gallengnge, sowie der Leber. Mittheil. aus den Grenz., xi, 1.

[57] Ueber Fieber bei Syphilis der Leber. Deut. Zeit. f. k. Med., lv, 176.

[58] Zur Kenntnis der fieberhaften tertiär-syphilitischen Organ-Erkrankungen. Centralbl. f. d. Grenz., ix, p. 641.

to 105° for two or three weeks. During several attacks the cervical glands had enlarged and, when personally seen, there was evidence of bronchial gland enlargement. The liver and spleen were not palpable and the blood count was normal. Death occurred two years later from puerperal infection, but, unfortunately, no autopsy was obtained.

As seen above, alternating pyrexia may be a symptom of many very different condititons. Regularly repeated attacks over long periods of time are most suggestive of tuberculous lymphomas, Hodgkin's disease, lymphosarcoma or other varieties of sarcoma. In any recurrent pyrexia, the possibility of disease of deep glands should be remembered. Rarely, as in the case recorded by Rolleston, or in the one here described, the liver may be, clinically, the sole organ affected.

TRUE INTESTINAL DYSPEPSIA.[1]

By Max Einhorn, M.D.,

PROFESSOR OF INTERNAL MEDICINE IN THE NEW YORK POSTGRADUATE MEDICAL SCHOOL, NEW YORK.

By the expression "intestinal dyspepsia" we understand conditions in which the digestive function of the intestinal tract is disturbed. The idea of testing the functions of the intestines in a manner similar to those of the stomach prevailed among clinicians for a long while, but its execution was attended with great difficulties. To Adolf Schmidt[2] belongs the credit of having elaborated a method to that effect. This well-known clinician introduced the test diet, known under his name, for the purpose of examining the feces. By means of this method, Schmidt and Strasburger[3] were enabled to discover a group of cases of intestinal dyspepsia, in which the starch digestion is particularly disturbed. They designated it fermentative dyspepsia.

Schmidt[4] has recently described the occurrence of functional achylia of the pancreas; by this he understands cases in which there is a malassimilation of the food, and a temporary lack of nuclear digestion—assigned by him as characteristic of the pancreatic secretion.

In a former paper[5] I have described similar cases, in which all nutritive substances were poorly digested. Yet I hardly believe it advisable to speak of achylia of the pancreas, because by achylia

[1] Read at a meeting of the American Gastro-enterological Association, at Atlantic City, N. J., June 3, 1907.

[2] The Test Diet in Intestinal Diseases. Translated by Charles D. Aaron, Philadelphia, 1906.

[3] Deut. Arch. f. klin. Med., 1901, lxix, 570.

[4] Functionelle Pankreasachylie, Deut. Arch. f. klin. Med., 1906, lxxxvii, 456.

[5] Further Remarks on the Digestive Bead Test for Ascertaining the Functions of the Digestive Apparatus. Jour. Amer. Med. Assoc., February 2, 1907.

we understand a complete absence of secretion. The conditions in the bowel are very complicated, depend upon many factors, and it is very difficult to judge which organ is at fault. However interesting the nucleus test may be, I do not think that it is of very great value in the recognition of disease of the pancreas, and I fully agree with Steele[6] when he says: "My clinical experience with the nucleus test does not entirely support Schmidt's claim for the method." I have only recently observed a case of tumor of the liver, with chronic jaundice, in which the nuclei at first were unchanged, but later—shortly before death—disappeared entirely. On the other hand, I have observed a case of achylia gastrica and grave anemia in which the pancreas was not involved, and in which the nuclear digestion was almost entirely absent. Besides, in all the cases of non-disappearance of the nuclei, it is possible that the pancreatic secretion is present, but its action inhibited by the presence of some other noxious substance (HCl, organic acids, etc.). It is, therefore, better to classify these cases under the heading of intestinal dyspepsia.

In the application of Schmidt's test-diet there are, however, some difficulties. It is often necessary to wait two to three days for the stool from the test-diet, and frequently the results are not easy to interpret. For these reasons Schmidt's method has not been adopted in general practice.

The bead test is easy to apply, and its results are sharply defined. Through a large number of examinations, which will soon be published, I have become convinced that the digestive functions of the bowel may be well judged by means of this test. There is, therefore, no reason why we should not utilize the test in the study of diseases of the bowel.

It is advisable to distinguish two large groups of intestinal disturbances: (1) Digestive disturbances which concern all three classes of food substances (albuminates, carbohydrates, fat): "dyspepsia intestinalis universalis." (2) Digestive disturbances affecting only certain classes of foodstuffs: "dyspepsia intestinalis partialis." This second group may be subdivided according to the varieties of foods, the digestion of which is disturbed: (*a*) Disturbed digestion of proteids; (*b*) carbohydrates; (*c*) fats; and (*d*) two classes of foods, namely, proteids and carbohydrates, carbohydrates and fats, and proteids and fat. These functional disturbances of the intestinal digestion may exist without appreciable anatomical change of the digestive apparatus, or they may be associated with lesions of the intestine. Occasionally subjective disturbances are found in the intestinal tract, in which neither anatomical nor functional deviations from the normal occur. These may be considered as true nervous intestinal dyspepsia.

[6] The Nucleus Test in Pancreatic Disease. Univ. Penna. Med. Bull., November, 1906.

In using the bead test, we must not imagine, if we find a substance in the beads undigested, that no digestion whatsoever of such substance may occur in the bowel. That would be wrong, for the same foodstuffs in liquid form may still be well digested. We can only conclude from this test that there is a considerable diminution of the digestive power for these substances.

I should now like to describe a few cases of functional intestinal dyspepsia which belong to both groups. The first two cases belong to group one (dyspepsia intestinalis universalis):

CASE I.—*Achylia Gastrica and Dyspepsia Intestinalis Universalis.* Israel R., aged sixty-two years, has been suffering for several years from a loss of appetite and digestive disturbances. Lately his trouble has increased and he complains of pain shortly after meals. His appetite has entirely disappeared. Patient sleeps poorly and complains a great deal of obstinate constipation. He has lost somewhat in weight.

Examination of the chest reveals normal conditions; in the abdomen, also, nothing abnormal is found. Examination of the stomach contents one hour after a test breakfast shows absence of HCl and rennet and a total acidity of four; very little fluid, and particles of roll scarcely changed. We have to deal here with a marked case of achylia gastrica.

The bead test[7] was given, with the following result: 4 beads are found after twenty-four hours; 1 after forty-eight hours; meat, fat, fish-bone, thymus, potato present; catgut was not found; nuclei in thymus have disappeared. Two weeks later the bead test was repeated and showed the presence of meat, potato, fat, thymus, and fish-bone.

The patient was put on a diet of milk, koumiss, raw eggs, soups, and strained gruels, and pancreon was given tentatively. He felt somewhat better, did not lose in weight, but his troubles did not cease. One and one-half years later he was still in the same condition: poor appetite, disagreeable sensations and constipation; however, he has not lost weight since January, 1906.

CASE II.—*Achylia Gastrica and Dyspepsia Intestinalis Universalis.* October, 1906. E. S. N., aged fifty-two years, complained for two years of digestive disturbances accompanied by severe attacks of diarrhœa and colicky pains. His appetite is moderate. For the last six months he has had constant diarrhœa and has lost about twenty pounds. A sojourn in a German watering-place has not given him any relief. Thoracic organs are normal. In the abdomen atony of the stomach is found. One hour after Ewald's test breakfast, a state of complete achylia is found. The bead test shows after twenty-one hours: thymus, meat, fish-bone, catgut, and half of the potato present. Nuclei and fat have disappeared.

[7] Archiv f. Verdauungskrankheiten, Heft i, table i, case 17, xiii

The patient was placed upon a diet of milk, koumiss, eggs, and fine gruels, and was given codein with tannigen. He gained slowly in weight and the diarrhœa was checked. In seven weeks he had gained eight pounds. Another examination of the stomach contents, as well as a bead test, was made. The stomach showed complete achylia, and the in bead test thymus, meat, catgut, and potato were found—everything else having disappeared.

The patient is still in about the same condition. He has not lost during treatment, and is still suffering more or less from diarrhœa.

CASE III.—*Dyspepsia Intestinalis Partialis.* Mrs. S., about thirty-two years old, rather corpulent, and with the appearance of good health, has been complaining for about a year. She has a disagreeable taste in her mouth. There is a feeling of pressure and fulness in the entire abdomen. She frequently belches and passes wind. She is always constipated, and must take strong cathartics. Even then the stool is insufficient and of a very offensive odor. The appetite is poor; she suffers from vertigo and tires very quickly. She does not sleep well. Recently she has been losing in weight.

Physical examination reveals nothing abnormal. Examination of the stomach contents is refused. The bead test shows after forty-six hours: thymus, meat, and fish-bone are present; potato, catgut, and nuclei have disappeared; fat bead was lost. Microscopically the stool shows a great number of large muscle fibers and smells very badly.

CASE IV.—*Dyspepsia Intestinalis Partialis.* Mr. M. complains of a feeling of fulness in the stomach and abdomen, much belching, great weakness, and persistent constipation. Examination shows systolic murmur at the apex beat; stomach extends a hand's width below the navel; right kidney is movable in the third degree. The stomach contents, removed one hour after breakfast, show the presence of free HCl, and a total acidity of 80. The diagnosis, therefore, is mitral insufficiency, enteroptosis, and hyperchlorhydria.

Patient was treated according to the usual methods. His general health improved, he gained in weight, but the constipation as well as the disagreeable sensations in the stomach and abdomen remained. The bead test was applied. The bead string passed after twenty-eight hours and showed the presence of thymus, fat, and half of the potato. Catgut, meat, fish-bone, as well as thymus nuclei, had disappeared.

The patient received takadiastase 0.3, three times daily. He at once improved. The sensations in the abdomen disappeared and the stool became nearly normal by the use of mild laxatives. The improvement has been permanent, and patient gained considerably in weight and strength.

CASE V.—*Hyperchlorhydria and Chronic Enteritis.* May 1, 1907. Oscar G., aged thirty-eight years, merchant. Previous history

negative. Six years ago he complained of gastralgia, at first over the appendix. Since then he localizes the pains somewhat higher (in the region of the gall-bladder). He took calomel and became worse, and at the same time the pains became more intense. These pains attack him now and again. He cannot breathe deeply when he has them. Between the attacks the patient feels a certain amount of discomfort in his abdomen, about two hours after meals. The bead test shows: beads regained after twenty-four hours—fat, half of the thymus and of the potato present. Nuclei and everything else have disappeared.

CASE VI.—May 9, 1907. Mrs. W., aged thirty years, was always well until seven years ago when she was married. She has had two children, and was perfectly well when she was pregnant. Seven years ago she began to have trouble with her digestion. She belches considerably and has a great deal of wind, and her bowels are constipated; they may be normal for awhile, then they become constipated and directly after again loose. Appetite is poor.

Examination shows that the chest organs are normal; the stomach reaches one finger's width below the navel; the right kidney is slightly movable. One hour after test breakfast HCl=O, total acidity=20. The bead test shows: string regained after twenty hours—meat, potato, thymus (nuclei disappeared), are present; everything else has disappeared.

CASE VII.—R. T. W., aged thirty-eight years, has been suffering for three years from severe attacks of pain in the upper abdominal region with subsequent vomiting. Between attacks the patient feels fairly well, but is very much constipated.

Examination revealed pronounced atony and ptosis of the stomach; otherwise nothing abnormal.

During an attack of vomiting free HCl and bile were demonstrated in the vomited matter. Ischochymia was not found. A week after the attack, when patient was feeling well, the bead test was used with the following result: after twenty-six hours—fat and potato are present; everything else had disappeared.

EPICRISIS. Both cases in group I shows that complete intestinal dyspepsia may exist for a long time without necessarily endangering the life of the patient. In both patients achylia gastrica was present. I do not, however, doubt that occasionally, even in the presence of gastric juice, a complete intestinal diyspepsia may be found. Case II to VII of group II are good examples of various special disturbances of the intestinal functions. Disturbances of carbohydrate digestion seem to be most frequent, and those of meat digestion the rarest. Future clinical observation of numerous cases will determine the subjective signs of these various intestinal dyspepsias, so that from them alone the diagnosis may be conjectured.

Therapeutically we can gather a few valuable points as a result of the testing of the intestinal functions. For instance, in complete

intestinal dyspepsia we must put the patient on a liquid or semi-liquid diet and administer pancreon and similar medicaments. In partial intestinal dyspepsia we can limit the amount of that variety of food for which the particular disturbance exists. Takadiastase, in doses of 5 grains three times daily, has been a valuable help in cases of amylaceous intestinal dyspepsia, as it seems to have removed the subjective symptoms in several cases of this kind. Pancreon in doses of 5 grains in disturbances of proteid and fat digestion seems to work well, although the results here are not so marked as in the former group.

PAROXYSMAL TACHYCARDIA.

By E. Schmoll, M.D.,

INSTRUCTOR IN CLINICAL MEDICINE IN THE COOPER MEDICAL COLLEGE, SAN FRANCISCO, CALIFORNIA.

The following study, based on 9 cases, is an attempt to show that in paroxysmal tachycardia we have to deal, not with a single pathological entity, but with different pathogenic forms.

Paroxysmal tachycardia is characterized by periods of extremely rapid pulse rate, of sudden onset and abrupt termination. It has been extensively studied by A. Hoffmann,[1] who showed that the increased heart rhythm is either double or four times the normal. Mackenzie[2] then showed that in some cases tricuspid insufficiency could be demonstrated during the tachycardia, while the heart action during the interval occurred in the normal auricular rhythm. Recently Schlesinger[3] has directed attention to the relation of paroxysmal tachycardia to pathological changes of the central nervous system.

The attacks are characterized by the sudden onset of tachycardia, its equally sudden termination, the absence, in the majority of cases, of pronounced subjective symptoms, except at the beginning and the end of the paroxysm. In 2 cases the attacks began with a feeling of chest-constriction analogous to the onset of a mild angina; in one other, choking and air-hunger were complained of; in the remaining cases distressing palpitation was the only sensation noted. Similar sensory disturbances, even more disturbing, marked the end of the tachycardia. The duration of the attacks was variable; the rapid pulse rate lasted in 1 case but ten to fifteen minutes at a time, while the longest attack lasted for five days.

From a study of the cases I am led to divide them into four etiological groups: (1) Cases of paroxysmal tachycardia occurring in patients with previously damaged heart; (2) cases of paroxysmal

[1] Ztschr. f. klin. Med., vol. 53.
[2] Study of the Pulse.
[3] Sammlung klin. Vorträge, 433.

tachycardia in patients affected by dysthyreosis; (3) cases of paroxysmal tachycardia in patients exhibiting central nervous lesions; and (4) cases of apparently functional character, so-called idiopathic group.

The following cases belong to the first group:

CASE I.—M. W., a female, aged thirty-four years, consulted me on account of dyspnœa on exertion, faintness, and vertigo. She had suffered from a mild degree of hemopilia, and presented changes in the heart and circulatory system. The pulse was regular, 80 per minute; the vessels normal; no arteriosclerotic changes; blood pressure above 150 mm. The apex beat was in the sixth interspace, 1 cm. outside the mammillary line, heaving in character. The heart dulness was increased, extending 2 cm. to the right of the sternal border. The heart sounds, excepting the second aortic, which was booming in character and strongly accentuated, were normal. The urine, on very frequent examinations, contained no albumin or casts. The backgrounds of the eyes showed no changes. The heart changes were considered secondary to the high pressure. While under treatment she developed a febrile attack, which was followed by a series of paroxysmal attacks, the pulse rising from the normal 80 to 100, to 150 to 200 beats to the minute. The attacks lasted from ten to fifteen minutes, and recurred repeatedly in twenty-four hours. This series of attacks lasted for six weeks, and finally subsided under roborating treatment and small doses of digitalis continued during the entire illness. The paroxysmal attacks subsided entirely for more than a year, but returned with a new febrile attack.

We had to deal in this case with the occurrence of paroxysmal tachycardia in a heart weakened by the strain of a high arterial pressure. The strain of the infectious process on the heart led to the attacks of paroxysmal quickening of the heart action.

CASE II.—C. M., aged fifty years, alcoholic, drinks beer to excess, formerly heavy smoker, present weight 230 pounds. His present sickness began about twelve years ago, when he suddenly dropped to the sidewalk on account of dizziness and violent throbbing in his chest. He was several months in a hospital where he had several attacks every day, lasting from fifteen minutes to six hours, during which the pulse frequently varied between 150 and 200 beats to the minute. Further series of attacks were brought on by drinking or over-exertion, and usually repeated themselves every second or third year. The present attack was brought on by the strain which the man was subjected to after the earthquake. The patient is very fat; slight exertion causes considerable dyspnœa. The pulse is regular and of low tension; the arteries are slightly thickened, but not calcified. The heart dulness extends 2 cm. to the right of the sternal border. The heart sounds are feeble and distant, the first is much shortened, and resembles the second. The

second pulmonic sound is slightly accentuated; the second aortic normal. During the paroxysm the heart is not enlarged; the sounds have assumed the embryonic rhythm; over the tricuspid area a soft systolic murmur is perceived and transmitted along the liver border. The veins of the neck, which before the attack showed a presystolic pulse, became very distended and pulsated violently, synchronously with the radial pulse, and were, therefore, of the ventricular type.

Another case of the first group was repeatedly seen in consultation with Dr. Gray.

Case III.—Mrs. A., aged, forty-five years. Has been suffering from attacks of frequent heart action, which were first noticed with an attack of cholecystitis; the pulse frequency during the paroxysm attained 200 to the minute, with typical onset and termination. The first attacks were mild and did not interfere with her household duties. In the last two years, however, the attacks have become so frequent that even the slightest exertion causes paroxysms of dyspnœa and tachycardia, so that she has been unable to leave her sick room. At the time I saw the patient she was wasted and anemic. A few days previously a relapse of her cholecystitis had occurred. Her pulse was fairly regular, varying between 80 and 90. The heart extended 3 cm. to the right of the sternal border. A systolic murmur could be heard over the apex and was transmitted to the axilla; a second systolic murmur was heard over the tricuspid area and was propagated along the liver border. The veins of the neck showed a systolic pulse; the liver was distinctly pulsating. While we were examining the patient an attack started, the pulse rate changing suddenly to 140 to 154 to the minute. The pulse during the attack was irregular, seeming to consist of a series of extra systoles.

The interesting facts in this group are that the heart lesion alone does not cause the symptom-complex, which originates only when a new weakening influence interferes with the action of the heart. As long as the heart has not sufficiently recovered the slightest provocation will lead to a paroxysm. The attacks, therefore, will occur in series. With the recovery of the heart muscle the tendency to attacks diminishes and the completely compensated heart does not present any attacks.

In the second group the paroxysmal attacks seem to be due to dysthyreosis. A number of observations have been published in which paroxysmal attacks complicated an exophthalmic goitre (Hoesslin,[4] Warden,[5] and P. K. Brown[6]). I have observed the occurrence of paroxysmal tachycardia in a case of dysthyreosis, and in a case of Dercum's disease (adiposis dolorosa) reported by Dr. J. B. Frankenheimer. The patient seemed to be absolutely unaware of

[4] Morbus Basedowii.

[5] Jour. Amer. Med. Assoc., 1906, p. iii.

[6] California State Med. Jour., 1906.

the rapid heart action. Whether this was due to her impaired mental faculites I could not decide.

Cases falling in the third group have received particular attention during the last few years. Numerous publications have demonstrated the frequent occurrence of tachycardia in pathological changes of the central nervous system. Nothnagel[7] first called attention to the occurrence of paroxysmal attacks with epileptic seizures. Numerous analogous cases have since been recorded. Schlesinger has observed epilepsy in 25 per cent. of his cases of paroxysmal tachycardia. He, however, draws attention to the fact that all these cases belonged to the symptomatic group of epilepsy caused by anatomical lesions.

The occurrence of paroxysmal tachycardia has been described after injuries to the head; other instances occurred with tabes; a typical case, combined with multiple sclerosis, has been described by Müller,[8] at the postmortem of which an extensive involvement of the vagus nuclei was found. A lesion of the medulla oblongata caused by a luetic endarteritis of the basilaris was found to be present in a case of Reinhold.[9] In some cases, tumor of the brain constituted the lesion (Pitres).[10] Tumor of the brain involving the frontal and parietal lobes around Roland's fissure, and causing paroxysmal tachycardia, was described by Reinhold. A case belonging to this group is the following:

Case IV.—A. B., aged sixty-six years, formerly alcoholic. He entered the hospital on account of emphysema and œdema of the legs. The patient showed marked arteriosclerosis in all the palpable arteries. The heart and aorta were slightly enlarged. Over the apex there was a mitral systolic murmur which disappeared with the improvement of the condition. The lungs were emphysematous, with many rales. In the hands and arms a very marked tremor was present, consisting of movements of flexion and extension of the hands and the fingers, occurring at the rate of 7 to 8 to the second, present most of the time, even in absolute rest. If he got excited, or tried to execute a difficult movement, the tremor became much more pronounced and resembled the tremor of multiple sclerosis. No ataxia; no Romberg sign. No paralysis or paresis of any muscle, but the muscles all over the body were hypertonic, most marked in the right leg. No nystagmus. Face mask-like. Speech monotonous, but otherwise undisturbed. Babinsky of right foot and an increased knee-jerk pointed to a lesion of the pyramidal tract; the abdominal reflex was absent on the right side, very feeble on the left. No disturbance of the bladder or rectum.

We have to deal, in this case, with an extensive arteriosclerosis combined with lesions of the nervous system. These point to a

[7] Ueber parox. Tachycardie, Wien. med. Blätter, 1887.
[8] Multiple Sclerose, Jena, 1904.
[9] Ztschr. f. klin. Med., vol. lix.
[10] Arch. clin. de Bordeaux, 1894.

non-systemic disturbance of the cord and brain. In many respects it resembles an atypical case of multiple sclerosis. The advanced age, however, and the existence of a marked arteriosclerosis point to the arteries as the cause of the nervous lesion (Oppenheim, Naunyn, Nonne, Luce, Demande). The attacks of paroxysmal tachycardia are probably due to a disturbance of the medulla oblongata, caused by the narrowing of the basilar artery, as in the case described by Reinhold.

Some interesting cases in which the paroxysmal tachycardia was caused by a lesion of the peripheral nervous system have been described by Schlesinger and Pal.[11] In Pal's case, several branches of the sympathetic nerve were involved in an adhesion going from the apex to the right innominate vein; whether this lesion, the influence of which would consist in an excitation of the accelerans, accounts for the symptom complex, seems to me to be very questionable, as the anatomical position of the accelerans in man has so far not been determined.

In Schlesinger's case the most important lesion discovered at autopsy consisted of an inflammation of the right vagus. During life the paroxysmal attack could be very easily stopped by compression of the right vagus, while compression of the left vagus seemed to be without any effect on the attack. In connection with the right-sided neuritis of the vagus, this observation proves the intimate relation of this lesion with the symptom complex. The pathogenesis of the attacks, however, is not made any clearer by this finding. In other cases in which a compression of the vagus was found a permanent tachycardia resulted (cases of Riegel, Ortner, Stix, Bois, and Sommer). It still remains to be explained why in some cases this lesion leads to a permanent tachycardia, in other cases to the paroxysmal form.

To the fourth group of apparently functional character belongs the following observation:

Case V.—J., aged sixty-eight years. Complains of attacks which, according to his conception, consist of a weakening of the heart action in so far as the heart has to contract twice to keep up the circulation. This conclusion he draws from the fact that his pulse rate doubles during the attacks. These began about twenty years ago, when the patient, who is a sea captain, got over-tired by a series of sleepless nights. The paroxysms usually begin with a feeling of constriction around the chest and choking; at the same time the pulse rate doubles; the attack lasts for a few minutes, and stops as abruptly as it started, while the pulse becomes slightly irregular for a few minutes. Deep breathing or pressure against the left side of the chest stops the attack. Sometimes he is free for several months, then again the attacks will come on several times

[11] Centralbl. f. innere Medizin, 1903.

a day. The examination shows that the heart is not enlarged, the blood pressure not increased; the kidneys work normally. The arteriosclerosis found is too slight to explain the tachycardia.

It seems that conditions in this disease are very similar to those seen in epilepsy, with which the paroxysmal tachycardia has numerous analogies, so many in fact that it has been considered as an equivalent. As in that disease, there are cases to be explained by an anatomical change of the nervous system, while in others the lesion is purely functional.

The mechanism of the attack was studied by tracings taken during normal heart action and during the paroxysms. This study leads to the conclusion that we have to distinguish two forms of tachy-

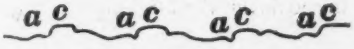


FIG. 1.—Normal venous pulse, showing auricular wave *a*, and transmitted carotid wave *c*.

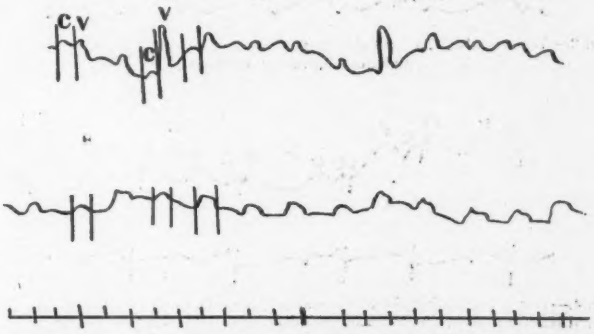


FIG. 2.—The upper tracing was obtained from the jugular vein, the lower tracing from the carotid artery: the time-markings correspond to one-fifth of a second. The tracing shows that the venous pulse commences synchronously with the carotid pulsation; that, therefore, during the attack the ventricular contraction is not preceded by an auricular contraction.

cardia: (1) Forms in which the auricular wave is missing, the jugular pulse being of the ventricular form; and (2) forms in which an auricular wave appears in the tracing obtained during the tachycardiac rhythm. In these cases the ventricular systole follows an auricular contraction.

Fig. 1, a tracing taken during normal heart action, shows the usual form of a feeble auricular venous pulse, the wave *a* indicating the auricular contraction, *c* the transmitted carotid pulsation; the wave *v* is not pronounced in this tracing. The heart action is regular, 72 to the minute. During the attack the character of the pulse changes entirely (Fig. 2). The feeble pulse has become very marked and has changed to the ventricular form. The simultane-

ously registered carotid pulse shows that no contraction occurs before the beginning of the ventricular systole indicated by the upstroke in the arterial tracing. The venous pulse begins only with the ventricular systole and consists of the usual two waves of the normal ventricular venous pulse. With the cessation of the attack the ventricular venous pulse is again replaced by an auricular, while the veins collapse.

The explanation of this change is found in irregularities which occurred occasionally during the normal heart rhythm (Figs. 3 and 4). These are clearly due to the occurrence of extra systoles. The absence of the auricular wave in the extra systoles of Fig. 3 shows clearly that no auricular beat occurs before the extra systolic pulse. Therefore, the extra systole originates below the auricle either from the ventricle or the atrioventricular bundle. Fig. 4 demonstrates

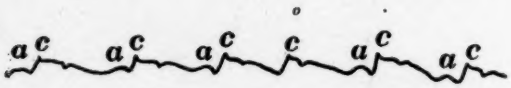


FIG. 3.—Venous pulse. At the point marked *o*, an extra systole occurs, in which the auricular contraction is missing.

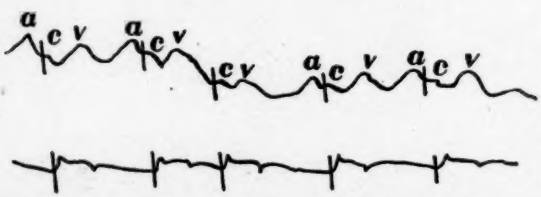


FIG. 4.—The upper tracing shows the venous pulse, the lower tracing, the carotid pulse registered simultaneously. At the point marked *o* an extra systole occurs without auricular contraction.

that during the extra systole the venous pulse shows exactly the same character as during the paroxysmal attack, and has changed to the ventricular type. The change of the venous pulse from the auricular to the ventricular form is, therefore, best explained if we assume that the paroxysmal attack is due to a series of extra systoles originating below the auricle. This view is corroborated by the comparison of the pulse rates. Fig. 5 shows the two different rates; the slow pulse rate was obtained by stopping an attack by deep inspiration. During the attack two systoles last 0.75 seconds, giving a pulse rate of 160. During normal heart action, taking immediately after the tachycardiac rhythm had stopped, a systole lasted 0.82 seconds, giving a pulse rate of 73 to the minute. We see that no relation exists between the two rhythms. The regularity of the rhythm during the attack is no objection to the extra systolic character of the attack, as the regular and rhythmical occurrence of

extra systoles has already been described by Pan[12] and Gebhardt.[13] The origin of the extra systole is indicated by the intermission following the extra contraction. Ventricular extra systoles may occur in two ways: either the pulse following the extra systole lasts until the next normal beat occurs, the time of the preceding systole plus the extra systole being equal to the time of two systoles; or the extra systole in a slow rhythm may occur without any disturbance of the normal rhythm. The extra systole is simply interposed be-

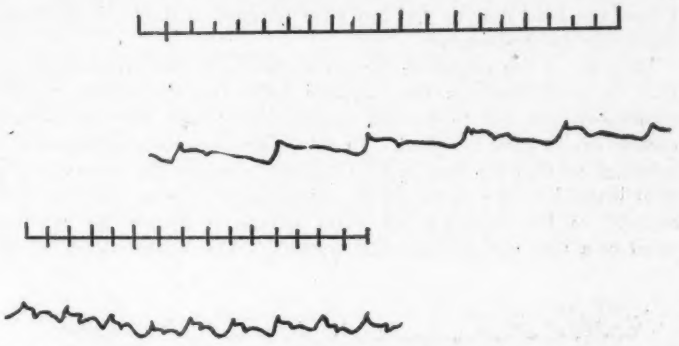


FIG. 5.—The upper tracing gives the carotid pulse during normal heart action, the lower tracing during the attack. Time-marking in fifths of a second.

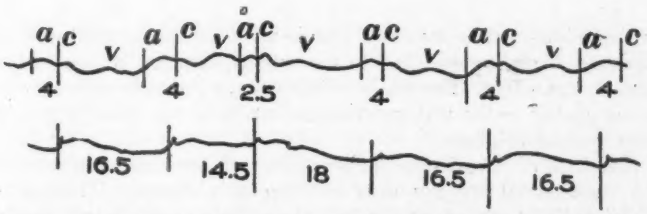


FIG. 6.—The upper tracing represents the venous pulse, the lower the arterial. At the point marked *o* an extra systole occurs characterized by a shortened *a-c* interval, proving its origin from the atrioventricular bundle.

tween two normal systoles. The measuring of the tracing shows that neither of these conditions applies to our case. The extra systole originates, therefore, from the bundle of His.

This view is corroborated by extra systoles observed at other times. In these an auricular contraction occurs preceding the extra-systolic beat, and if one measures the distance *a–c*, one finds that this interval is very much shortened (Fig. 6). This shortening of the interval has been shown by Hering[14] to be characteristic

[12] Ztschr. f. exper. Path., vol. ii.
[13] Arch. f. klin. Med., vol. lxxxi.
[14] Ztschr. f. exper. Path., vol. ii.

of the extra systoles originating from the atrioventricular bundle. An extra stimulus originating from this point progresses to the auricle on one side, to the ventricle on the other. According to the exact location of the place producing the stimulus, both cavities will either contract at the same time or the auricle will contract after the ventricle, or the auricular contraction will precede the ventricular extra systole, but in a shortened interval. In the reproduced tracings we find two of these instances, the simultaneous contraction and the auricular preceding the ventricular in a shortened interval. I have not been able to find any sure instance of the auricular wave following the ventricular.

Because of the origin of the extra systole in the His bundle, we find in most tracings the diastole following the extra systole, prolonged, but not to the full length, after which the next normal systole would have followed. In some instances the prolongation is minimal, so that the next systole follows in nearly the same interval as if instead of the extra systole a normal systole would have preceded. In this instance the extra systole is simply the starting point of a new series of normal systoles. The conservation of the

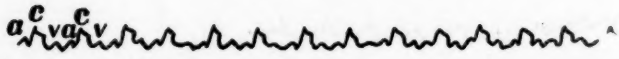


FIG. 7.—The venous pulse during the attack, with the typical three waves: *a*, the auricular; *c*, the transmitted carotid; *v*, occurring at the closure of the semilunar valves.

normal rhythm after the extra systole would point, according to the experiments of Engelmann,[15] to the venous sinus as the cause of the extra contraction. The study of the venous pulse, however, points unmistakably to the atrioventricular bundle as the point where the extra systoles originate.

The form of paroxysmal tachycardia with auricular venous pulse was represented by my case of Dercum's disease. During the period of heart rhythm 140 to 180, the pulse was absolutely regular, and consisted of the three usual waves of the venous pulse—*a*, *c*, and *v* (Fig. 7).

In many instances a change occurs while the heart beats in the rapid rhythm; each second pulse beat becomes very small, to be followed again by a very strong pulse beat. The rhythm of the heart is not disturbed by this allorrhythmia, which represents the typical pulsus alternans first described by Traube, who differentiated it from the bigeminal rhythm by the fact that the intermission following the feeble beat is prolonged in the bigeminal rhythm and normal in the alternating (Fig. 8).

The alternating pulse has been considered by Wenckebach[16]

[15] Pflüger's Archiv, vol. lxii.

[16] Arrhythmie, Leipzig, 1903.

as characteristic of a lesion of contractility. His view was based on the experimental work of Engelmann and Hoffmann.[17] The measure of contractility is given by the height of the contraction, as at each systole the heart contracts with a maximum contraction. The contractility is destroyed by each contraction and recovers slowly during diastole. After a short diastole the contractility does not fully return and a feeble systole results, while a long diastole permits a strong contraction. If one reduces, experimentally, the contractility of the heart muscle, either by causing a frequent heart action (Engelmann) or by stimulating the vagus (Hoffmann), a typical alternation occurs, while the duration of the systole decreases. The cause of the alternation has been found to depend on the fact that the normal heart stimulus is never absolutely rhythmical; it may occur too early in diastole and a feeble contraction ensues. This systole, being feeble, will last a shorter time than a normal systole; the next diastole, therefore, is lengthened, causing a strong systole, which, however, will again lead to a shortening of the diastole. A continuous alternation will be the result.

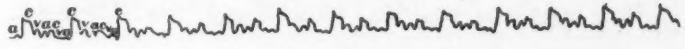


FIG. 8.—A typical alternating pulse.

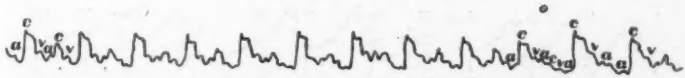


FIG. 9.—An alternating pulse, showing to the right (point *o*), a systole occurring too early and leading to a disturbance of the alternation.

Fig. 8 illustrates these changes (1 second being equal to 17.5 mm.). The *a* waves occur rhythmically, as well as the *c* waves, at an interval of 0.35 second; the systole in the strong beat lasts 0.17 second; the diastole, 0.18; in the weak beat the duration of the systole is 0.12 second; of the diastole, 0.23.

In Fig. 9 is another instance of the alternating pulse (1 second = 20 mm.). *c* and *a* waves are again rhythmical, each heart evolution requiring 0.3 second. The systole of the strong beat requires 0.175 second, the diastole 0.125 second; the systole of the weak beat lasts 0.1 second, the diastole 0.2 second. At the place marked *o* the pulse beat occurs about 0.25 too early, the following systole is, therefore, extremely feeble, the preceding diastole having been shortened. A very strong systole follows with the effect that the next diastole is so shortened that contractility does not recover sufficiently. The ventricle, therefore, is unable to open the aortic valve, and only the auricular wave appears in the pulse tracing.

[17] Pflüger's Archiv, vol. lxxxiv.

In both tracings an alternation in the auricular action may be noted. The strong auricular beat, however, corresponds to the weak ventricular, and the weak auricular to the strong ventricular. In other tracings not published here the alternation occurs in the auricle and ventricle at the same time. Similar tracings showing an alternation in the auricular action have been published by Volhard,[18] who states that in alternating pulse the small wave in the pulse tracing is of shorter duration than the strong one, for the following reasons: The weakly contracting ventricle will need a longer time to overcome the diastolic aortic pressure; the closure time is prolonged; besides this, the weak pulse wave progresses more slowly in the arterial system than the normal (Extraverspatung). Several tracings in which, with a rhythmical heart action, the duration of the weaker pulse wave in the radical is shorter than that of the strong pulse wave, corroborates his view. That this, however, does not apply to all the cases is clearly shown by Figs. 8 and 9; whereas the retardation of the auricular, as well as the ventricular, wave is clearly shown in Fig. 10

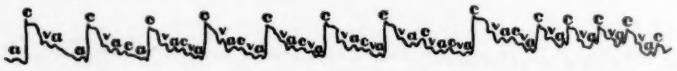


FIG. 10.—The transition from an alternating to a regular rapid pulse.

FIG. 11.—The occurrence of extra systoles.

The recovery of the heart from a state of diminution of contractility is shown in Fig. 10. In the beginning the strength of the heart is so diminished that the ventricle is unable in each second beat to open the arterial valves, and only an auricular wave appears; with a partial recovery an alternation sets in, which finally goes over into a regular rapid pulse.

At other times we meet with periods of irregularity which cannot be explained by lesions of contractility. A typical example is given in Fig. 11, showing the jugular pulse. At the beginning the pulse rhythm is regular, about 100 to the minute, each systole lasting 0.6 second. After four pulses an irregularity occurs, showing a premature contraction consisting of three small waves. The first of the waves is undoubtedly the auricular wave, followed by wave *c* and *v*. The interval between the *a* waves measured in millimeters (3.5 mm.=0.2 sec.) is the following:

[18] Münch. med. Woch., 1905.

A1–A2—11.0 mm.
A2–A3—11.0 mm.
A3–A4—11.0 mm.
A4–A5— 8.0 mm.
A5–A6—11.0 mm.
A6–A7—11.5 mm.
A 7–A 8— 8.0 mm.
A 8–A 9—11.5 mm.
A 9–A10—11.5 mm.
A10–A11— 8.0 mm.
A11–A12—11.5 mm.

Thus, in three periods the auricular systole occurs too early in the cardiac cycle; an abortive systole ensues, as the contractility has not sufficiently recovered during the shortened diastole. This abortive systole is followed by a regular systole in the normal interval. At times the extra systole occurred so early in the diastole

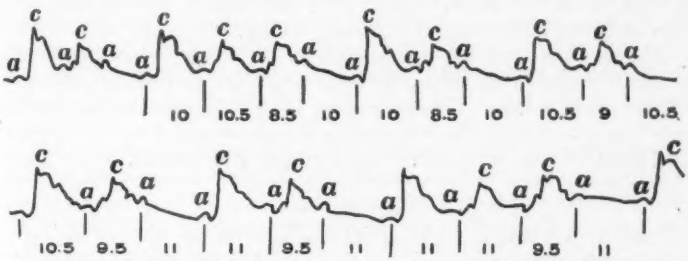


FIG. 12.—The occurrence of extra systoles, in which the contraction was insufficient to open the aortic valve; only an auricular wave shows, therefore, in the tracing.

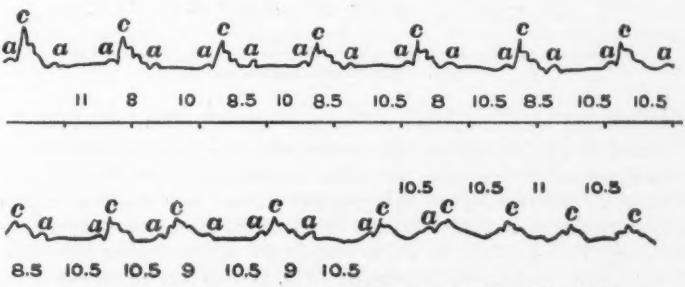


FIG. 13.—The regular occurrence of extra systoles simulating heart-block.

that the ventricle was unable to contract sufficiently to open the aortic valve. Only an auricular wave appeared in the pulse tracing (Fig. 12). Evidence that the ventricle contracted could not be obtained graphically, as no apex tracing could be secured, but it was shown clearly by a booming sound heard over the heart just after this auricular wave. The character of the sound was typical of its extra-systolic origin and differed entirely from the feeble auricular sounds heard in heart block.

In some instances these extra systoles without ventricular waves occurred regularly, giving the impression of heart block (Fig. 13).

One can easily see that the time between an extra systolic auricular wave *a* and the next auricular wave is equal to the normal time of one heart evolution shown at the end of the tracing—thus proving the extra-systolic character of these contractions.

The similarity to heart block due to a lesion of a conductivity is increased by the influence which the extra systole has on the interval *a–c*, which we are accustomed to consider as a measure of the conductivity (Wenckebach, Mackenzie). During the normal rhythm of the heart the interval *a–c* is equal to 0.2 seconds (Fig. 14, 4 mm.; 2, 0.2 sec.). In the extra systole the interval *a–c* is only 0.05 second; in the following systole 0.1; the normal interval of 0.2 is only obtained in the second following systole.

The shortening of the interval *a–c* in the extra systole points, as in our first case, to the atrioventricular bundle as the place whence the extra systole starts. The shortening in the next following systole can be explained by the rest during the prolonged diastole, so that the conductivity is restored during this contraction. The only

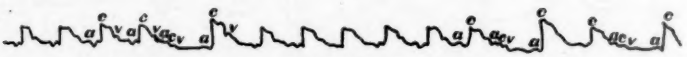


FIG. 14.—Shortening of the *a–c* interval during the extra systole, and in the following systole.

FIG. 15.—Transition from a slow rhythm with interposed extra systoles to a regular rapid rhythm. (Time marking in seconds.)

point which speaks against the origin from the His bundle is the absence of any compensating interval after the extra systole, a fact which points to the venus sinus as the starting point for the extra stimulus. The study of the tracings of our first case, in which the stimulus proceeded from the His bundle, shows, however, conclusively that in such an extra systole the interval after the extra beat is not necessarily prolonged (Fig. 3). This, in conjunction with the shortening of the *a–c* interval, seems to prove that in this case, too, the tachycardia is caused by extra systoles starting from the atrioventricular bundle. The changing of the rhythm to a tachycardiac attack is clearly shown tin Fig. 15. During the slow rhythm the auricular waves occur during the diastole between ventricular beats, occurring too early, and, therefore, being extra systoles. At this point an extra systole occurs very much too early, but is followed by two very small waves, *c* and *v*. The next systole follows at an even shorter interval, again producing a ventricular systole. The rhythm then becomes very rapid, the ventricle responding to each stimulus. The changing of the rhythm

is clearly due to a series of extra systoles. The regularity of their occurrence does not speak against their extra-systolic nature, as we have seen the regular occurrence of extra systoles in Fig. 8. Similar tracings with rhythmical extra systoles have been published by Gerhardt and Lommel.[19]

Tracings showing the pathogenesis of the attacks were only obtained in these 2 cases, but in other cases auscultatory evidence of the extra-systolic character of the paroxysmal attack could be obtained. It would be entirely hypothetical to try to explain the attack from a physiological standpoint. Whether disease of the vagus nerve alone or in combination with an irritation of the accelerans may cause such an attack is difficult to determine in the absence of physiological experiments. Further investigations may clear up the question, in which conditions the point of origin for the stimulus changes from the venous sinus to the atrioventricular bundle.

The argument presented in this paper, however, emphasizes the pathological importance of the atrioventricular conducting system. It is interesting to note that paroxysmal and permanent bradycardia, as well as paroxysmal tachycardia, can be referred to a lesion of the His bundle.

DILATATION OF THE HEART.[1]

By Thomas A. Claytor, M.D.,

Professor of Therapeutics and of Clinical Medicine, George Washington University, Washington, D. C.; Physician to the Garfield and the University Hospitals, Washington, D. C.

It is not my intention to go into a detailed discussion of dilatation of the heart, but only to touch upon some of the more important points, more especially the etiology and treatment.

Dilatation of the heart is associated with either a thickening or a thinning of its walls, more commonly the former, and may be looked upon as an index of the disproportion between the intracardiac pressure and the resisting power of those walls. One or all of the cavities may be affected.

Etiology. The majority of instances of cardiac dilatation may be said to result from one of the following factors, operating either singly or collectively: (1) An increase in the amount of work to be done by the heart, as in general arteriosclerosis, chronic nephritis, valvular disease, overstrain, etc; (2) an impairment of the power of the myocardium from degenerative changes, toxic conditions, etc.; and (3) failure of the cardiac muscular tone, as seen in some

[19] Arch. f. klin. Med., vol. lxxxii.

[1] Read at a meeting of the American Climatological Association, Washington, D. C., May 7, 8, and 9, 1907.

instances of severe nervous shock, etc. Thus we see in arteriosclerosis and in chronic nephritis, hypertrophy and dilatation of the heart due to increased demands upon this organ. In valvular lesions of all varieties there is almost sure to occur more or less dilatation, usually with hypertrophy. Examples of overstrain are to be seen in athletes and in those whose occupations require great muscular effort. Oarsmen and long-distance runners necessarily tax their hearts to the utmost. The cardiac pulsations are greatly increased in force and in frequency to supply the increased demands of the muscular system and to accommodate the rapid return of the blood to the heart, but this may not be sufficient. Besides, the mechanical overfilling of the cardiac chambers, which produces a severe strain on the contractility of the cardiac muscle, there are also the fatigue products which probably have a toxic effect on the muscle fibers. With this combination at work, there is small wonder that the heart gives way under the strain, and dilates in some instances. I am aware, however, that there are some observers who do not believe that a sound heart ever dilates from excessive muscular exertion alone.

Among the more important causes of myocardial degeneration are the acute infectious diseases, such as diphtheria, influenza, and rheumatism, if we may class the latter as such. According to Lees[2] myocarditis is far more common in rheumatism than in diphtheria and influenza, but much less dangerous, and the microscope shows much less destruction of the muscle fibers. Not a few deaths result from acute dilatation in diphtheria or shortly after apparent recovery, and many instances of weak heart finally presenting the picture of dilatation date back to an attack of epidemic influenza. A number of writers have called attention to dilatation in typhoid fever, notably Louis, Andral, Gunsburg, Wunderlich, and Stokes. The condition may be general or noted on either side of the heart. Romberg[3] found considerable dilatation of the right ventricle and right auricle with a contracted and hard left heart. A typical example of cardiac dilatation in a case of typhoid fever came under my observation last fall, developing in the fifth or sixth week of the disease and rapidly ending fatally.

In the more intense forms of anemia, cardiac dilatation is the rule, and probably accounts for many of the murmurs which we are wont to call hemic. Myocardial degeneration seen in those past middle life is most commonly due to failure of the blood supply of the cardiac muscle, resulting from sclerosis of the coronaries.

After considering the many definite and tangible causes of dilatation, such as myocardial degeneration, valvular lesions, nephritis, etc., there still remains a fairly large class in which we are not able

[2] Brit. Med. Jour., 1901.
[3] Erkrank. d. Herzmuskels bei Scharlach., Diph., u. Typhus, Arch. f. klin. Med., xlvii.

to find perfectly satisfactory explanation. Here we must fall back on the nervous system and say that the cause is loss of muscular tone; indeed, this seems not by any means an improbable solution—in fact it is urged by Colbeck[4] that all forms of cardiac dilatation may be directly traced to loss of muscular tone. By muscular tone we mean that state of tension in which the muscles are held—which is dependent on the nerve supply.

It is a well-known fact that severe shocks, joy, grief, or any severe nervous strain may cause a dilatation of the heart, and, as Broadbent has said, death may result actually from a broken heart. Immediate death under such circumstances, however, is prabobly due to cardiac inhibition. I am inclined to believe that small doses of opium, which often seem to act so satisfactorily in dilatation, produce results largely through the soothing effect upon the nervous system. Cheimisse[5] states that Marmorstein reported two instances of cardiac dilatation from shock during the rioting in Odessa. The patients were neurotic, and the sight of murder and pillage was the immediate cause. Many such examples are to be found in literature.

It is quite conceivable that under prolonged severe exertion even the perfectly normal heart might, and we know does, become exhausted and loses temporarily its muscular tone. In the majority of instances this form of dilatation is rather quickly recovered from, but not always. It is a well-known fact that the training which an athlete goes through for a strenuous competition is to give the muscles, and the heart muscle in particular, a chance to hypertrophy. The young, from their mode of life, are always more or less in training; hence the violent strains which their hearts are called upon to bear, do no specific harm, except, I believe, in rare instances; but it is a vastly different matter when a man past forty, who has given up active exercise for some years, is called upon for some violent effort, such as a sprint of a couple of squares to catch a car, or who, because of a too irascible temper, becomes involved in a bodily conflict. If this happens to one whose heart is under the influence of nicotine or some such toxic agent, or who has a pre-existing heart trouble, such as a valvular lesion or a myocardial degeneration, dilatation of a serious nature may quickly develop with all the usual indications.

The exciting cause may be any unusual muscular or mental effort. I recently saw a prominent lawyer who, though well advanced in years, had always been a man of remarkable vigor, who brought on the symptoms of dilatation by the preparation of a long and important brief. He had just concluded his arduous task when he was suddenly seized with dyspnœa and oppression in the cardiac region. I found the heart considerably enlarged, acting very irregularly,

[4] Lancet, 1904.

[5] Semaine méd., 1907, No. 9.

and a mitral systotic murmur present. Whether this murmur was due to a true valvular lesion or to a relative insufficiency from dilatation I am unable to say, as he left for his home in the West as soon as he had partially recovered.

Another gentleman, whom I had the opportunity to observe for a number of years, suffered a severe dilatation from over-fatigue of body and mind during an active political campaign, and a second very acute attack, which nearly cost him his life, was the immediate result of rather vigorous abdominal massage. In this case there had been for many years completely compensated mitral and aortic insufficiencies, with but little enlargement of the heart.

Again, the symptoms of dilatation may be brought on by an acute illness in those who, though the subjects of valvular lesions or some other disorder of the heart, have acquired perfect compensation. I had such an instance under observation while writing this paper. A woman aged forty years, who has for a long time shown the physical signs of a mitral stenosis, developed a bronchopneumonia, with a very harassing cough. After a few days of constant coughing, marked orthopnœa, with œdema of the lungs, developed. Examination of the heart showed a loud systolic murmur in the tricuspid area, in addition to the pre-existing mitral stenotic bruit. Caffeine in liberal doses gave fairly prompt relief, and the wall of the right ventricle so far regained its tone that the systolic murmur was scarcely audible at the last examination.

One of the more recent instances which has come under my observation was in the case of an old lady who suffered from a myocardial degeneration. One night she got out of bed, slipped on the floor, and, in a violent struggle to regain her feet before anyone should find her up alone, brought on a marked dilatation, from which she almost died. It is useless to multiply examples of this well-known condition.

Symptoms. Sleeplessness is not infrequently the first symptom to attract the attention of the patient. Sometimes it is referred to the violence of the heart's action or to an uncomfortable feeling of nervousness, or to a cough, evidently due to faulty circulation. In other instances there is actual dyspnœa or even orthopnœa. It is a strange fact that these sufferers often rest quietly for some hours after retiring, only to be awakened in the early morning by one of the above-mentioned symptoms.

The possibility of cardiac insufficiency should always be borne in mind when insomnia develops. A stimulant in such instances is often the best hypnotic. I well remember one patient in whom a small dose of digitalis produced such prompt sleep that it was mistaken for an opiate. There is usually complaint of weight and oppression over the precordium—seldom actual pain. Sometimes the dilatation seems to make itself actually felt, the patient saying that he feels as though the heart were too big for the chest.

The pulse is usually rapid and, not uncommonly, arrhythmic. Dyspnœa at first only on exertion, later becomes more or less constant. Cyanosis and œdema of the lungs may develop, the latter being one of the earliest and most persistent symptoms, as evidenced by cough with seromucous expectoration, which may be slightly pinkish or quite bloody, depending on the amount of congestion. In acute dilataton œdema of the lungs is one of the most urgent symptoms and not infrequently appears to be the immediate cause of death. General œdema is usually of later development, when there is no longer any doubt as to the diagnosis. Many of those whose hearts are undergoing gradual dilatation suffer chiefly from gastro-intestinal disorders—flatulent dyspepsia or nausea, due to congestion of the abdominal organs; and it is often difficult to convince them that the heart is the cause of their trouble. The liver becomes congested and often greatly enlarged and painful to pressure, even if there be no complaint of heaviness in the right hypochondrium. Congestion of the kidneys results in scanty, more or less albuminous urine, in which casts are usually to be found.

Diagnosis. The diagnosis is based upon the presence of the above-named symptoms and upon the following physical signs: The whole precordium may seem to throb with each systole of the ventricles, when there is an associated hypertrophy of much magnitude; while in instances of dilatation with thinning of the walls there may be no visible impulse whatever, or only the merest undulatory wave in the neighborhood of the apex. The jugular veins may be distended and may pulsate. If the right ventricle is dilated, the epigastrium may pulsate. The apex beat is nearly always displaced to the left, and downward if the left ventricle is involved. By laying the ulnar surface of the hand parallel to and to the right of the sternum, a fair idea of the extension of the heart to the right may be obtained by the impulse which is often palpable to this sensitive part of the hand, although one is likely to get a slightly exaggerated impression of the size of the heart by this method. My attention was first called to this valuable point by C. H. Hoover. In percussion of the heart, I wish to lay great stress upon the advantage of the palpatory method over all others; its accuracy is often very gratifying. The cardiac dulness will be found to be increased to a greater or less degree, depending on the dilatation. An accurate determination of the area of dulness is of the greatest importance, and at the same time requires more skill and practice than any other part of the examination. There may or may not be heard endocardial murmurs, due to true lesions of the valves, but there is likely to be present the systolic murmur of a relative insufficiency of the mitral or of the tricuspid valve or of both. Time alone will prove this point. The disappearance of the murmur of a relative insufficiency is always encouraging, as it is an indication that the cardiac chambers are returning to the normal size.

The sphygmomanometer has been rather a disappointment as an aid to diagnosis in diseases of the heart. It is of value, however, in giving warning of possible danger ahead. For instance, the discovery of an abnormally high blood pressure at once suggests the presence of conditions, such as arteriosclerosis or chronic nephritis, which will sooner or later be likely to produce hypertrophy with dilatation, and we are able to direct the life of the patient accordingly. The use of this exact method of estimating the pressure also makes one much more accurate in the examination of the superficial arteries in determining the real force of the pulse. A point which was at first a surprise to me was the high blood pressure so frequently observed in spite of the very evident symptoms of cardiac insufficiency. I mean especially in the first few days of what might be called an acute dilatation, when there was dyspnœa, œdema of the lungs, arrhythmia of the pulse and other indications of circulatory insufficiency. As the condition improved the pressure fell, and the reduction occurred in spite of the constant administration of digitalis and cardiac stimulants other than the nitrites. These observations were upon cases of dilatation with hypertrophy. The elevation of pressure under such circumstances would appear to be due to exaggerated efforts of the heart and vessels to re-establish the circulatory equilibrium.

Differential Diagnosis. The two conditions with which dilatation might be confounded are simple hypertrophy and pericardial effusion. The former requires but little consideration as the symptoms are not the same, unless the walls of the heart have begun to relax, when it falls into the class now under discussion. A pericardial effusion, however, is by no means so easily differentiated from dilatation, as the symptoms may be practically the same. In the former the cardiac impulse is generally less distinct, the first and second sounds weaker, and most important of all—there may be heard a pericardial friction rub, even though there exists a large effusion. It must be borne in mind, however, that the two conditions may co-exist. In effusion the area of dulness is of the classical irregular dome-shape, the apex being upward, and extends lower down, depressing the left lobe of the liver in some instances. The relation of the extent of dulness to the position of the apex beat, when it can be felt, is of importance. In effusion the dulness extends to the left and below the position of the apex beat. Dulness in the right fifth interspace, as pointed out by Rotch, is a valuable sign of effusion, as is also the broadening of the area of dulness toward the base of the dome when the patient assumes the sitting posture. If there still be doubt, the question may be quickly settled by the use of the fluoroscope, when the apparatus is available; the dilated heart will be seen to pulsate while the effusion will remain stationary.

TREATMENT. In an endeavor to relieve this conditon it is necessary to bear in mind the two cardinal objects: To lessen the amount of work which is required of the heart, and to increase the power of the heart to do its work. The first may be accomplished by absolute bodily and mental rest, by a light diet, by active purgation, by relaxing the peripheral vessels, and by bleeding. The second may be accomplished by the administration of cardiac stimulants, by baths, by judicious exercises, etc.

Prophylaxis is worth much in cases of beginning dilatation. If these patients can be got under control when the first indications manifest themselves, many attacks may be warded off by advice as to overstrain, either mental or physical. If men with large interests and women with excessive household or social cares can be induced to lighten their loads of responsibility; if heavy eaters can have their appetites controlled, much may be accomplished without recourse to medicine.

Even after serious symptoms have actually developed, much may be done without cardiac stimulants. Some of our patients yield promptly to rest in bed, a dose of calomel or blue mass, followed by salines. If this fails to restore the circulatory equilibrium, digitalis is turned to by the vast majority, and I, too, usually give it the preference; but caffeine is, in my opinion, a very close second and not infrequently is superior. I think that I have noted this superiority especially in cases of high blood pressure, which would be easily explained by the difference in physiological action of the two drugs. But at this point I want to emphasize the fact that digitalis in some cases is indispensable, in spite of high blood pressure, in spite of the most marked calcareous degeneration of the arteries, as far as they can be felt. In some instances our best efforts along these lines will fail, and the symptoms even grow worse—cyanosis and dyspnœa increase, nausea develop with extreme restlessness, and the heart's action become more irregular and rapid. These are the cases which require more heroic handling, and these are the cases, if properly selected, which are often benefited by bleeding. The patients who are best adapted to blood-letting are the plethoric—more usually men who, though suffering from some heart lesion, have, through careful dietetic and hygienic regimen, been made to increase in weight and strength, and who, by some indiscretion, have been smitten in the midst of comparative health.

Some prefer wet cups or leeches, and they may be very beneficial. Incidentally, I might say that I cannot see why their application over the precordium, in preference to any other area, should be of especial advantage, unless they should also act as counterirritants. My own experience has been with venesection; hence, I prefer the very simple method of opening a vein in the forearm and drawing off from 8 to 16 ounces of blood. The results are in some instances most gratifying. I have seen the cyanosis improve at once, the

nausea disappear while the blood was still flowing, and the patient express himself as much more comfortable. This method of relieving the over-distended heart appeals to me as being one of the most rational at our command, and yet it is surprising how few ever resort to it. By unloading the venous circulation, the overfilled heart is enabled more completely to empty itself, and the overstretched muscle fibers are once more allowed an opportunity to contract to somewhere their normal dimensions. After bleeding, cardiac tonics produce results which previously seemed unattainable.

I shall not mention the names of the army of drugs which have been used in dilatation of the heart, but will content myself with the mention of one more, which, if properly given, will be found most useful—that is opium. These patients are often possessed with that spirit of unrest, that condition of general wretchedness which it is hard to describe, but which is perfectly familiar to us all. For this symptom-complex there is nothing so useful as small doses of morphine. I have found as little as $\frac{1}{32}$ grain every four hours most beneficial; not only does it quiet the nervous system, but it seems to stimulate the heart, and in most instances appears to do no harm. I shall not take up the treatment of dilatation by exercises and baths. A discussion such as the present would hardly be complete without some mention of the most acute forms of dilatation. In these the anxious, terror-stricken expression, livid skin, thready pulse, with cold and clammy sweat, indicates that death is imminent. The free use of nitroglycerin has, in some instances, seemed to be life-saving, and I have rather learned to rely upon it under such circumstances. Caffeine is especially useful when œdema of the lungs is pronounced. In fact nitroglycerin, caffeine, and digitalis may be given at the same time, as their promptness of action is about in the order named, so that the effect of the first two will have entirely disappeared before the third makes itself felt. Nitroglycerin should, in my opinion, be reserved for emergencies such as the above and for the attacks of great oppression which are likely to come on from time to time in the less acute cases of dilatation. Its continued use is depressing. I have not mentioned strychnine because I have rather lost faith in it, having observed better effects from other remedies.

Diet. Upon this point there are two widely different opinions. The one, that only liquids should be given; the other, that a dry diet is preferable, on the ground that the more liquid is taken into the system the more will be taken up by the vessels, and consequently the greater amount of fluid will have to be moved by the already overladen heart. After trying both methods, I have concluded that the dry diet is to be preferred, unless there are decided uremic symptoms to be considered. Especially is this true when there is, as is so often the case, a tendency to tympanites.

A RESUME OF THE PHYSIOLOGY OF THE KIDNEY, WITH A VIEW TO THERAPEUTICS.[1]

By V. E. Henderson, M.A., M.B.,
LECTURER IN PHARMACOLOGY AND THERAPEUTICS, UNIVERSITY OF TORONTO, TORONTO, CANADA.

A review and, as far as possible, a fair summary of the state of our knowledge of the physiology of the kidney seems to me to be quite worth while, especially in view of its great importance to those who are combating disease; because of the very rapid advances and the many changes which our knowledge of the functions of the kidney, synthetic, analytic, and secretory, have recently undergone; and because the old-time theories proposed by Ludwig and Heidenhain are, with this increase in knowledge, being gradually modified by their respective followers, and in many important points approaching each other; though it must be admitted that the theory of Ludwig, as was to be expected from its inherent simplicity of explanation, is being widely deviated from. I will discuss at the close of the paper the probable constructive lines for a new theory. First, I wish to adduce the important facts.

I. The Internal Secretion. The chief arguments in favor of this theory suggested by Brown-Séquard are as follows:

1. It has been observed in both men and animals that occlusion of both ureters leads but slowly to death (men have lived frequently fourteen to sixteen days), and that death ensues in man (it is harder to judge of this in animals) without marked symptoms of uremia, often with hardly a symptom that could be classed as uremia. In Fowler's summary of 93 cases, more than 66 per cent. showed no marked uremic symptoms. On the other hand, in animals and in man, when accidentally a single functional kidney has been removed, death occurs more rapidly (four to six days in man), though at least 1 case is on record in which a man lived eleven days; nor do all cases show marked uremic symptoms, though they are more common than in the first group. There is, however, it must be noted, a very marked difference in the severity of the operations for ureter closure and kidney removal in animals, and in man the ureters have rarely been closed by operative interference, and then only in severe operations. This fact must be seriously considered when considering the value of the differences between the two groups of cases.

2. Bradford and others have noted very marked wasting of the body and increased loss of nitrogen accompanying the polyuria which supervenes when five-sixths of the kidneys are removed. This, too, may be ascribed to an internal secretion.

3. The pharmacological experiments of Brown-Séquard and

[1] Read at a meeting of the American Therapeutic Association, Washington, D. C., May 7, 8, and 9, 1907.

others who tried to reduce an impending or existing uremia produced in animals by double nephrectomy by injections of (*a*) glycerin extract of kidney, or (*b*) defibrinated blood from normal animals, taken either from kidney veins or the general circulation. Brown-Séquard himself was the first to experiment with the glycerin extract. His experiments seem to have been few in number and are not reported in detail. He himself subsequently appears to place more reliance on his pupils' work and upon general considerations such as the above. Ajello and Parascandalo operated on twelve dogs who died in from four to forty-eight hours; of ten other dogs which, after similar operation received glycerin extract injections, one lived four days, six others three days, the other three died in from forty-eight to fifty-two hours. This is not very convincing, especially when the controls died so early—four hours even; much longer survivals than forty-eight hours have occurred in similar experiments reported by other observers. Their rabbit experiments are not more convincing. The work of Meyer, a pupil of Brown-Séquard, whose work is considered by the latter as conclusive, is still less satisfactory. In one series of experiments he chose the cessation of dyspnœa, as recorded graphically, as a sign of improvement. Neglecting the fact that the method of recording might lead to deception, the criticism used is hardly a satisfactory one, as is urged with reason by Tigerstedt and Lewandowsky. His experiments are only five in number—three dogs and two rabbits. He used for injection blood of normal animals. Meyer, and also Vitzou, carried on a series of experiments in which the length of postoperative life with and without injections of blood was compared. Animals receiving injections had certainly longer postoperative lives, but that this was due to an internal secretion is rendered doubtful by the experiments of Chatin and Quinard, who showed the blood serum, which one would expect to contain the secretion, had absolutely no effect in prolonging the animals' lives. They have a longer and more complete experimental series than have either of the others. It seems that either the internal secretion must be carried by the corpuscles or that the corpuscles aid in prolonging the postoperative lives, if, indeed, they were prolonged in the experiments reported above.

4. Therapeutic experiments with extracts of kidney on uremic and nephritic persons are reported as successful by Dieulafoy, Tiessier and Frankel, Jacquet, Concetti, and Chiperowitz. A careful analysis of such cases as I have been able to see are not convining. Comparatively sudden changes for the better are not rare in nephritis. The treatment seems to have fallen into disuse since, in the literature available, I have found no reference to it since 1898.

5. As shown by several observers, uremia has supervened in nephritis without evident nitrogen retention. This is an unexplained fact.

I think it unnecessary to consider the experiments of Tigerstedt and Bergmann, so completely nullified by those of Lewanowski, nor the evidence that some have tried to deduce from the variations in hemolytic and toxic properties of serum and urine in cases of nephritis.

To sum up, I think that Brown-Séquard's suggestion has been rendered not more, but rather less, plausible than when first communicated. Great loss of functional kidney substance does lead to an abnormal metabolism, but this by no means proves an internal secretion.

II. Synthetic and Analytical Functions. The mention of the paper of Barcroft and Brodie, who showed that increase in the excretory function of the kidney led to an increased consumption of oxygen and increased giving off of carbon dioxide in the blood, leads me to speak of the other known chemical activities of the kidney.

1. *Synthetic.* I need but to recall that the kidney can synthetize hippuric acid from glycerin and benzoic acid, salicyluric acid from salicylic acid and glycine. Also carbonic acids of many other nuclei in addition to that of the benzene nucleus, such as, furan, thiophene, and pyridin can be excreted in similar combinations. That this is a function of the kidney and doubtless of the tubules, has been still further confirmed by the success of Abelous and Ribaut in isolating to a certain extent the ferment responsible therefor.

2. *Analytic.* Schittenhelm has distinctly shown that the kidney contains a ferment which is able to split uric acid into urea, and also ferments which desamidize and oxidize other purin bodies. It is possible also that kreatinin, which, as Landois showed, is toxic with symptoms resembling uremia, may be formed by dehydration in the kidney from the nontoxic kreatin. Doubtless other synthetic and analytic functions will be discovered, and it may well be that their disturbance will, in large part, explain the causation of uremia.

III. Tubular Excretions. Nevertheless, these functions are, on the whole, subordinate to the main function of the excretion of urine.

1. The paper of Ebstein and Nicolaier, and, more convincingly, those of Sauer and of Anten, show that uric acid is excreted by the cells of the convoluted tubules and also, possibly, by those of the ascending loop of Henle. Undoubtedly those cells which carry on synthetic and analytic activities will also cast their products into the tubular lumen, and we will not be far astray if we localize these functions also in the tubule. Some experiments performed by Tropp show that such a synthesis as that of hippuric acid is not accompanied by any increase in water excretion. I have lately tried in three experiments to find an increased flow of urine when uric acid is secreted in large quantities, but as yet all experiments have been completely negative. Greatly increased uric acid excre-

tion was accompanied by a decrease, not an increase, in water. Phloridzin is known to be a poison which attacks the tubules, and some evidence exists that the passage of dextrose into the urine after the use of this poison is accompanied by loss of water. This may also be true of such poisons as cantharidin and possibly calomel. The pigments are also probably excreted by the cells of the convoluted tubules, as injected foreign pigments have been shown to be by Hober and Königsberg.

Attention must also be called to the fact that the urine leaving Bowman's capsule is alkaline, as shown by Dresser, while in the convoluted tubules it becomes acid. This is probably due to an increase in the free hydrogen ions, owing to the passage of CO_2 which, in the experiment of Barcroft and Brodie, does not appear in the venous blood in proportion to the oxygen lost by the arterial blood.

2. The recent papers of Bainbridge and Beddard and of Cullis and Brodie, if confirmed, as is probable they will be, will prove that the tubules in the frog, at all events, can excrete water, urea, chlorides, sulphates, probably kreatinin and phosphates, and dextrose when there is hyperglycemia or when poisoned with phloridzin. Caffeine sodium benzoate also seems to stimulate to excretion (note this body contains two substances which should influence tubules). It is, of course, doubtful how far we can apply to man results obtained on frogs in which the relations of the blood supply are so different, the tubules having, as well as the arterial, a secondary venous blood supply from the lower limbs; still, if we do so, the following points in the experiments of Cullis are of importance: the tubules on a venous supply did not excrete except when stimulated; neither phosphates, chlorides, nitrates, nor sulphates acted as such a stimulant; urea was a weak or doubtful stimulant, while phloridzin and caffeine sodium benzoate were the successful stimulants. The work of Loewi and Schmid would also go to show that sugar is excreted by the tubules when poisoned with phloridzin. The increase in urine flow accompanying it they consider to be due to a prevention of water absorption.

Accepting the observations of Cullis and Brodie on frogs, it is apparent that the diuretic salts, sulphates, phosphates, carbonates, if in excess in the body, must be got rid of by the glomeruli. This is the view most generally accepted, though Meyer and others do not fully concur in it. Before, however, we consider the excretion of salts, I wish to draw attention to the fact that under any but the most extreme experimental conditions an excess of such salts cannot occur in the blood without at once introducing osmotic pressure differences between the blood and the tissues, and that these are at once done away with, first, by water passing into the blood; and, second, by salts passing into the tissues. Very rapid salt absorption will lead to hydremia.

3. *Inorganic Salts and Urea.* The following facts are to be noted in regard to urea and nitrogen excretions: Urea occurs in normal urine in higher concentration than in the blood plasma (100 c.c. of urine often contains as much urea as 2 liters of plasma).

The more rapid the flow of urine, in general, the smaller the percentage of urea; the greater the daily quantity, the lower the percentage; but the total daily amount of urea will vary only with the daily nitrogenous katabolism.

Especially in cases of nephritis, the output of urea does not necessarily keep pace with its intake nor with katabolism (heaping up of non-coagulable nitrogenous bodies has been shown to occur in the blood), and this in cases in which water excretion appears normal; in other words, nitrogen retention with normal water excretion. The cause of such retention does not necessarily reside in an inability on the part of the kidney to excrete urea, though it may be so in some cases. Such nitrogen retention may persist for a long time (as in a case reported by Draper, for thirty days, and amount to 146 of nitrogen) without uremic symptoms.

4. *In regard to chlorides:* retention of chlorides in nephritis leads almost at once to a retention of water. Retention of salt has amounted to 40 to 50 grams, and was accompanied by proportionate increase in œdema. So many cases are now on record in which chloride retention has been shown to be the cause of water retention, that Marie has been led to frame the following hypothesis: that at first, on retention occurring the tissues are able to fix and retain a certain amount of chloride; when this is surpassed, water retention must occur. With restored chloride excretion, water also is given off. But the failure to excrete chlorides is rarely or ever absolute; retention occurs only above a certain daily intake. If the salt intake be reduced below this limit chloride elimination occurs, and, with it, water (Widal, Halpern, Claus, Plaut, and Reach). Increase in intake sometimes seems to hinder excretion.

5. *Sulphates and phosphates* may, like the chlorides, vary independently of their intake, and also of the nitrogen output, or temporarily of the water. Such massive retentions as are reported for chlorides, however, do not occur, and, as a whole, their daily amounts vary with the food intake and daily katabolism.

All these salts are present normally in the urine in larger amounts than in the plasma, but the more rapid the urine excretion, the lower their percentage, until it may happen that in extreme cases traces alone of chlorides occur. The urine may also come to have a higher freezing point than the plasma, that is, contain a much lower salt percentage (Dreser, Brodie, Henderson, Frey, etc.).

The excretion of a urine with a lower salt content than the normal blood for a long time—several hours in animal experiments—as shown by Achard and Paisseau, Reichel, Brandstein, and others, causes definite degenerate changes in the convoluted epithelium.

Leopold has also shown recently (his paper much needs verification) that feeding to rabbits and dogs a not excessive amount of salt daily (rabbits from 0.05 to 1 gram), also led to changes in these same convoluted tubules. He also showed that the changes caused by phosphates were much more marked.

6. *Water.* In regard to the excretion of water even the most ardent advocates of the secretory activities of the tubules suggest the glomerulus as the site of the main water excretion. The phylogenetic development of the kidney suggests it; the glomerulus at first is projected into the body cavity near the inner end of the neophrostome, whose mouth is lined with cilia. It must also, however, be noted that it was then the main, if not the sole, excretory apparatus for other body waste. The histology of the kidney suggests it. The afferent vessel to the glomerulus is larger than the efferent; the efferent vessel breaks up about the lower tubules to form a second capillary network. Hence the blood pressure in the glomerulus must be high; the pressure in its capillaries higher than elsewhere in the body. The epithelium of the glomerulus is thin and very flat, and probably syncytial. It is not gland-like in appearance.

Increased water production is favored by (*a*) an increase in blood flowing through the kidney (Starling, etc.). This must be qualified by the reservation that the blood may not be too concentrated. Observations are on record in which, though the blood flow through the kidney increased when caffeine was given, yet little or no secretion occurred, and it has been shown that in these cases the percentage of water in the tissues was low (Henderson). (*b*) Increase of blood pressure from the arterial side, if not accompanied by a decreased flow through the organ, increases the flow. Impeding venous outflow decreases water excretion. There is a certain minimum blood pressure below which no urine is excreted. This minimum varies with the composition of the blood—the more hydremic the blood, the lower the minimum; it is probably between 30 to 40 mm. Hg. in man (Starling, Henderson). Caffeine has been shown to dilate the vessels of the kidney, and, at the same time, by its heart action the blood pressure does not fall (Loewi, Brodie, etc.). (I believe that only when the kidney vessels are greatly dilated before injection does dilatation not occur.) That means an increased flow of blood through the kidney under equal or increased pressure. It may fail as a diuretic if the patient be poor in water. Other purin bases act as diuretics in the same way. As pointed out above, caffeine may possibly lead to increased activity of the tubules as well. Digitalis is not a diuretic in normal individuals, but is invaluable in those cases in which the circulation is poor. With improvement in the circulation comes diuresis. It may fail, of course, in those œdematous cases in which the œdema is due to chloride retention. Mercury

salts, as pointed out above, are poisons for the tubule cells, and no doubt act as such. Hydremia is apt to dilate the vessels of the kidney, but is not constant in its action. (*c*) The presence in the blood of increased amount of salts, with high osmotic equivalents, sulphates, phosphates, carbonates, as well as the occurrence in increased amounts of salts with not such high osmotic equivalents, chlorides, dextrose, nitrates, increase the flow. All these act largely, first, by increasing the water content of the blood; second, by carrying water with them into the tubules and retaining it there (Loewi, etc.); and third, evidence is also to be found in many papers that salts in excess may also cause a local dilatation of the vessels of the kidney (Magnus, Brodie, etc.). (*d*) The addition, by the tubules, of dextrose or other crystalloids increases the flow.

Reversal of the above conditions, decrease in blood flow, in the amount of salt in blood stream, etc., will decrease the flow of urine.

Finally, in nephritis, damage may lead to a primary inability to excrete water, and, on account of osmosis, salts must be retained, and thus greatly decrease the amount of urine.

Having thus briefly, and necessarily imperfectly, but I hope not unjustly, reviewed the facts in regard to kidney function, may I be allowed briefly to sum up the facts as they stand, and contribute in a word or two a picture of the production of urine. First, the cells of the tubules do undoubtedly excrete urates, hippurates, pigments, and, possibly, creatinin. They are permeable, and, in the frog, as in man, may excrete water, chlorides, urea, phosphates, sulphates, under stimulus, and, under still more abnormal circumstances, dextrose (phloridzin hypercemia). Second, the urine leaving the tubules, though usually more concentrated than the plasma in salts and urea, under a rapid flow more closely approximates to it in salt composition, and may even in some cases become much more dilute than the plasma, as in, experiments spoken of above and in diabetes insipidus. The first of these facts, great concentration, may be explained by very great water absorption by the tubules, which, there is evidence to show, does occur. The second, only by very greater absorption of salts by the tubules, and this is especially hard to understand in cases such as diabetes insipidus, in which the body really seems to need water. This necessary supplementary explanation, taken in conjunction with all our more recent knowledge of living animal membranes, many subsidiary difficulties not mentioned in the paper, and facts in regard to the definite excretory functions of the tubule spoken of, so overloads and modifies Ludwig's conception of the excretion of urine as to make it no longer tenable, even if we make, as has been pointed out to be necessary, the modification of understanding for "filtration" "diffusion modified by pressure." Then must we, with Heidenhain, say the glomerulus and tubules secrete. It appears to me to be a matter of defini-

tion. Heidenhain, when he said secrete, meant, I think, secretion, such as is carried on by other glands.

Let us take a typical secreting gland, such as the submaxillary, and see what secretion means in its case. It is, first, supplied with nerves, stimulation of which causes a flow of secretion even without increased blood flow. The kidney appears to have none such. Such a gland, on appropriate stimulation, nervous or chemical, secretes, and even against considerable pressure, even if the blood supply be poor; in the extreme case even if it be absent. The kidney in rabbits fails absolutely to secrete if the blood pressure be lower than 30 mm. Hg. and the blood normal. Caffeine is looked upon as the most efficient chemical stimulus we have (salts and water cause changes in the blood and urine which may greatly alter the conditions); yet, as I have shown, when the body is poor in water, caffeine fails as an excitant to secretion, though it brings about the necessary vascular changes. Such a gland, furnished with normal blood, will secrete when stimulated against a pressure many times the blood pressure of its vessels. This the kidney fails to do, although the glomerulus does not alone excrete, and there is no very great distance from the convoluted tubules to the ureter, but here, it must be noted, that the excretion of the tubules is not necessarily accompanied, as shown by Tropp and myself, to be accompanied by much water. Change in renal blood pressure is exactly and instantly followed by the pressure in the ureter, and a fair flow of urine, with a high blood pressure, will give a greater ureter pressure than a faster urine flow with a low blood pressure. We have, therefore, in the kidney a different type of secretion. Why not drop the word, with its associations, and say excretion?

If both these old theories have proved to contain fallacies, is there any theory which can be propounded to explain the production of urine? I believe we shall soon be able to answer in the affirmative. May I be permitted to indicate what I think to be the probable constructive lines. On the one hand, we may believe that the glomerulus excretes water, urea, chlorides, and possibly other salts, and that it must be so delicately adjusted as to respond to very small variations in the amounts of these substances in the blood and have a selective excretory activity for each substance, which may be either increased or decreased by disease, etc. Sulphates and phosphates may be added by the tubules with such other substances as the urates. It may even be that each constituent is added by a different secreting mechanism. It might also be suggested that the excretory activity regulated the amount and distribution of the blood flow. On the other hand, the researches of Kahlenberg may lead us to a new physical conception of semipermeable membranes, and of diffusion, and may thus open up for us entirely new conceptions in regard to animal membranes and the role that osmosis plays within the body.

I feel myself unfortunate that in this review of the kidney's functions I have not been able to indicate in any way the probable cause and method of the treatment of uremia.

The futility of trying to form soluble compounds of uric acid, and so aid its being washed out of the kidney, seems to me to be disclosed in the above. Even the highly soluble piperazin compound, or, as shown by Nicolaier lately, the formaldehyde compound, are not excreted as such, but are broken down and excreted as less soluble urates. Probably any beneficial action that piperazin had was due to its action in dilating the kidney vessels and so increasing the blood flow through the kidney.

That digitalin and the purin bodies at times fail is not astonishing when one considers that neither causes a specific secretion, but their action is limited by the state of the bloodstream and its richness or poorness in water.

Further, the inability and failure of digitalis and of caffeine to cause diuresis even in œdema, when salt retention is present, is abundantly evident. It is in those cases that decreased in salt intake has given such astonishing results.

That salines, acetates, and sulphates, etc., act as diuretics when caffeine and calomel fail, is not astonishing when one realizes the changes in blood and in composition of urine which occur when they are exhibited. That they may fail when caffeine is efficient is equally lacking in peculiarity.

Most important of all, I think, is the fact that with our lack of knowledge of the kidney, and how it carries on its function, it is not to be expected that we will be successful, as indeed we are not, in forcing the kidney to excrete when it is diseased. The fact that when there is chloride retention an increased intake may cause more marked retention, taken altogether with the facts mentioned above, that Riedel, Brandenstein and Achard have shown that undue amounts of water cause damage to the kidney, as does excretion of undue amounts of salts, as shown by Leopold, should lead us, especially in nephritis, to guard the kidneys from labor of every kind that can be avoided.

OTITIC BRAIN ABSCESS.[1]

By Edward Bradford Dench, M.D.,

PROFESSOR OF OTOLOGY IN THE UNIVERSITY AND BELLEVUE HOSPITAL MEDICAL COLLEGE, NEW YORK; AURAL SURGEON TO THE NEW YORK EYE AND EAR INFIRMARY; CONSULTING OTOLOGIST TO ST. LUKE'S HOSPITAL AND THE NEW YORK ORTHOPEDIC DISPENSARY AND HOSPITAL, NEW YORK.

The study of cases of intracranial suppuration complicating otitis media is always interesting. It has been my pleasure to bring before the society at various times cases of this character. In presenting 2 cases at this meeting, I have taken the liberty of appending an analysis of 102 cases of cerebellar and 100 cases of cerebral abscess, with special reference to the symptomatology, the route of infection, the presence or absence of optic neuritis, and the value of various methods of operative procedure. Unfortunately my own 2 cases terminated fatally. One was a case of cerebellar abscess and the other a case of abscess in the inferior frontal convolution.

Cerebellar Abscess. The case of cerebellar abscess occurred in a young boy, thirteen years of age, who entered the hospital suffering from what seemed to be an acute exacerbation of a chronic suppuration involving the right ear. The patient had severe pain, some œdema over the mastoid, extending down into the neck, a discharge from the ear, and some headache. A radical operation was done upon the right ear, and an epidural abscess over the sinus was found. No grafting was employed. The patient did well for two days, when he was found to have a polymorphonuclear leukocyte count of over 84 per cent. and a leukocytosis of 33,600. There was also some elevation of temperature, and on dressing the wound a suppurating sinus was found extending down the neck. This was drained by a counter-opening and the patient seemed to progress satisfactorily for a day or two, when his temperature again rose to about 104°, and he became lethargic, stupid, and complained of some headache. An examination showed no muscular paralysis, and the optic disks normal. Owing to the fact that there was no evidence of suppuration within the cerebrum, and because there had been an epidural abscess about the sinus at the time of the primary operation, it seemed to me that the most probable site of suppuration was an abscess of the cerebellum. The patient was again placed upon the operating table, and an incision made in the cerebellar dura in front of the lateral sinus. Considerable turbid serum was evacuated, and a probe could be passed into an abscess cavity in the cerebellum. The cerebellum was then explored behind the sinus, the dura incised, and a director inserted into the posterior

[1] Read at a meeting of the American Otological Society, Washington, D. C., May 7, 1907.

opening could be made to touch a probe passed into the opening in front of the sinus. Gauze packing was introduced into both openings, and the patient returned to bed. He died within twenty-four hours after the operation.

In this case there had been absolutely no evidence of intracranial suppuration until the patient's temperature rose suddenly and he became dull and stupid. Without question, the cerebellar abscess had existed for some time. Had symptoms been present at the time of the radical operation undoubtedly he might have been relieved by operation.

As we can only learn the symptomatology of a given disease from the study of the histories of a large number of cases, I thought that it might not be out of place to analyze 102 cases of cerebellar abscess with special reference to the symptomatology. These cases have been collected for me by my assistant, Dr. Charles E. Perkins, to whom I wish to express my sincere thanks.

Route of Infection. In a study of these cases the first point to be noticed is the method of infection. The route of infection was through the petrous portion of the temporal bone in 30 cases, through the lateral sinus in 30, in 4 the infection seemed to travel through the mastoid, in 3 the cerebellar abscess was secondary to a cerebral abscess, while in the remaining cases the route of infection could not be made out. It would seem, therefore, from these statistics, that cerebellar abscess occurs with about equal frequency as the result of infection of the lateral sinus and of infection of the petrous portion of the temporal bone, that is, through the internal auditory meatus, or through the aquæductus cochleæ and aquæductus vestibuli. The cases secondary to an abscess of the cerebrum are, naturally, exceedingly rare.

Symptoms. When we come to the consideration of the general symptoms, it is interesting to note that the most prominent and constant symptom is headache. This occurred in 71 of the cases, and was seldom localized; it was simply complained of as a general headache, and was not referred to any particular region of the skull.

Another prominent symptom of cerebellar abscess is vomiting, which occurred in 54 cases, in which a record is made of the presence or absence of this symptom. In 1 case the notes state that there was "no vomiting." In 1 of the cases which came under my own observation vomiting was present, although it was not very severe, and occurred rather early; in 3 other cases it was not noted.

Vertigo was present in 30 of the 102 cases. In 5 of these the patients had a tendency to fall to the side opposite the lesion. This was present in the case which I reported last year. In the case which I have just reported the patient could not walk at the time when the cerebellar symptoms first appeared, and consequently the character of the vertigo is not noted.

Nystagmus was noted in 17 of the cases. This symptom would therefore, seem to be a rather uncommon complication of cerebellar abscess.

The pulse was slow in 40 of the cases in which any record of the pulse is given. The slow pulse would naturally be an indication of an intracranial complication, and the pulse rate could not be taken as a differential sign in locating the abscess in the cerebellum or in the cerebrum. In 26 of the cerebellar cases the temperature was subnormal, while in 5 the temperature was high.

Retraction of the muscles of the neck was noted in 12 cases.

Stupor occurred in 44 of the cases. This stupor varied from a mental lethargy to a state of hebetude, and, in marked cases, to coma. This symptom is ordinarily present, to some degree, in all cases of intracranial suppuration, the degree of the stupor usually depending upon the degree of intracranial pressure.

The condition of the muscular reflexes was noted in 10 cases only. In 6 the knee-jerk was increased on the affected side, and in 1 case there was slight increase on the opposite side. In 3 cases the knee-jerk was absent. In the other cases the condition of this reflex is not noted.

Regarding the condition of the pupils, in 9 cases the pupils were noted as "unequal." In 5 the pupil on the affected side was dilated, and in but 1 case was the opposite pupil dilated.

Strabismus was noted in 9 cases. In 1 case the eyes were turned to the opposite side, in 7 the character of the strabismus was not noted, and in 1 case it is marked as "internal" strabismus. As the sixth nerve is the nerve usually affected in these cases, strabismus, when present, is usually internal.

Respiratory symptoms were noted in 9 cases. In 3 respiration is noted as "Cheyne-Stokes," while in 6 respiration ceased at the time of operation, and it was necessary to complete the operation under artificial respiration.

Regarding the condition of the fundus oculi, out of the series of 102 cases optic neuritis was present in 34 cases, absent in 37 cases, and in 31 cases the condition of the optic papillæ is not stated.

The analysis of these symptoms, while perhaps not of great value, will, I think, serve to establish more clearly in our minds the characteristics of cerebellar abscess.

Mortality. Regarding the mortality of cerebellar abscess, out of the 102 cases death occurred in 69, while 33 patients recovered.

Operative Treatment. The method of operation practised in these cases was as follows: Out of the 102 cases collated, in 45 the abscess was opened behind the lateral sinus; 25 of these resulted in cure, and 20 in death. In 11 cases the abscess was opened in front of the lateral sinus; in 4 of these cure ensued, and in 7 death occurred. In 46 cases the method of operation was not stated; in 4 of these cases cure ensued, and in 42 death resulted.

The method of operation in any of these cases must depend upon the probable route of infection. I say "probable," because in many cases the avenue of infection can only be surmised. I think we can lay it down as a fairly good rule, however, that, unless at the time of operation the surgeon can trace the route of infection from the lateral sinus, an exploratoy opening in the cerebellum should be made anterior to the sinus, in view of the fact that if evidences of infection by way of the sinus are absent the most probable channel of infection has been either through the internal auditory meatus or through either the aquæductus vestibuli or the aquæductus cochleæ. In either of these latter events the abscess could be more easily evacuated by incising the cerebellar dura in front of the lateral sinus. In some cases the lateral sinus is located sufficiently far backward to permit of a free incision in the cerebellar dura in front of it. In other cases, in which the sinus lies far forward, it is almost impossible to make an incision of any length through the cerebellar dura in front of this vessel, and the posterior route must be chosen. In a number of cases—as in the case reported herewith—it may seem wise, after evacuating the abscess by the anterior route, to make a counteropening through healthy cerebellum behind the sinus, in order to secure perfect drainage.

Cerebral Abscess. I have also to report a case of cerebral abscess which occurred in my practice two years ago. The patient was a woman, aged forty-seven, who gave a history of an acute inflammation of the left ear ten years previously. There had been no aural symptoms during this interval until about two weeks before I saw her, when she had an attack of the grip, accompanied by pain in the left ear. The left ear had been discharging about ten days prior to the time I was called to see her. Upon my examination, the left drum membrane was found to be bulging and red. There was a small perforation in the upper portion of the drum membrane, affording insufficient drainage. There was no evidence of any previous middle-ear suppuration, as far as I could determine from my examination of the ear. At the time of my first examination the left mastoid was excessively tender. A free myringotomy was performed. A smear of the discharge showed the Friedländer bacillus. As the mastoid tenderness did not disappear in spite of incision of the drum membrane, a complete mastoid operation was done forty-eight hours after I first saw the patient. The mastoid cells were found to be extensively involved and the lateral sinus covered with granulation tissue. The sinus wall was extremely thin, and just below where it was covered with granulations the sinus was accidentally wounded in removing the overlying bone. The hemorrhage was easily controlled and the mastoid wound dressed in the ordinary manner. The patient did perfectly well for six weeks, at which time the mastoid wound had almost entirely healed. During this period the temperature had been practically normal, and

aside from the fact that she did not gain flesh after the operation, there were absolutely no unusual symptoms marking her convalescence. One month after the operation, following a dressing, the temperature rose to 100°. The following day she suddenly became aphasic and the temperature rose to 102.5°. The patient was seen by several eminent physicians—one a prominent neurologist—and all agreed that the symptoms were due to thrombosis of a branch of the middle cerebral artery supplying Broca's convolution and the island of Reil. Ophthalmoscopic examination was negative. An examination of the blood showed 84 per cent. of polymorphonuclear cells, with a leukocytosis of 11,400. The temperature ranged between normal and 102° for one week, then dropped to 100°, and, although the aphasia did not improve, the general condition of the patient seemed to be better. Owing to the high polymorphonuclear count, I was inclined to believe that the patient was suffering from a cerebral abscess, and a prominent surgeon was called in consultation. He rather shared my opinion, but did not consider the symptoms positive enough to warrant exploratory operation. Blood counts, at frequent intervals, showed a leukocytosis varying from 11,000 to 17,000 and a polymorphonuclear count ranging from 79 per cent. to 85 per cent. After several consultations it was decided not to operate, and, consequently, no operation was performed until the day before death. Two days before her death the patient had a severe chill, complained of headache, and the temperature rose to 101°, but fell the next morning to normal. The day before operation the temperature was normal, but the patient complained of considerable headache. She, however, was perfectly rational. On the evening of this day the temperature began to rise, the patient complained of severe headache, and on the morning before death she had a temperature of 104°. I operated immediately, and found an abscess in the inferior frontal convolution and the island of Reil. Symptoms of meningitis were present when the patient was put upon the table, and I regarded the condition as absolutely hopeless when the operation was performed. An examination of the abscess cavity showed this to be very large, and involving the frontal lobe. The abscess was so large that it could not possibly have developed during the time that the patient was under my care. I am, therefore, inclined to believe that she was suffering from a latent brain abscess, which became re-infected at the time of her acute otitis. Had the operation been performed earlier in this case, I think the chances for recovery might have been good.

The symptomatology of cerebral abscess is far from clear. Through the efforts of my assistant, Dr. Chas. E. Perkins, I have been able to analyze 100 cases of cerebral abscess, with special reference to symptomatology. Some of my own cases are included in this list, but the report embodies chiefly the work of other observers,

as most of my own cases have been reported from time to time, and have been intentionally omitted from this list.

Out of these cases, the suppuration was on the right side in 41 cases, on the left side in 42; both ears were involved in 1 case, and in the other cases the side is not reported; 20 followed an acute middle-ear suppuration and 77 followed a chronic middle-ear suppuration. In the remaining 3 cases the duration of the suppuration is not reported.

The *route of infection* in these cases was as follows: Through the tegmen tympani in 40; secondary to epidural abscess in 6; secondary to sinus thrombosis in 6; through the mastoid antrum in 6; secondary to infection through the squama in 2, while in 9 no bone defect was found; 1 case was secondary to a cerebellar abscess (Case 48).

Symptoms. Regarding the symptoms, 77 complained of headache and in 44 vomiting was a prominent symptom. The pulse was slow in 37 cases and rapid in 1. Vertigo was present in 32 cases—a rather unusual symptom for a cerebral abscess. The temperature was high in 7 cases and either normal or subnormal in 20. Coma and stupor were noted in 31 cases. Mental dulness was noted in 20 cases and aphasia in 10 cases. Optic neuritis was present in 32 cases, absent in 20 cases, and in the remainder the condition of the optic disk is not mentioned. Nystagmus was present in 4 cases. Pupillary symptoms were present in 17 cases. General convulsions were present in 5 cases. Paralytic or paretic symptoms were present in 17 cases. In 15 cases the motor disturbance was on the side opposite the brain abscess; in 2 it was on the same side as the abscess. The degree of motor disturbance varied, from slight impairment of motion to hemiplegia. I have seen hemiplegia occur in one or two of my own cases, and it has also been noted in the reports of one or two other cases embodied in this article. In my own case, and in one of the others reported, the hemiplegia only came on after operative interference. Therefore, it might quite as well have been due to a traumatism inflicted at the time of the operation as to the original abscess. In one case, however, namely, that reported by Hansberg,[2] there was complete hemiplegia of the opposite side.

The reflexes were abolished in 1 case and exaggerated in 7.

Operative Treatment. The results of operation show 52 cases resulting in cure and 48 fatal cases.

It is interesting to note the method of operation in these cases. In 41 the abscess was opened through the tegmen, and of these 27 resulted in cure, and 14 in death; 37 cases were opened through the squama, and of these 18 resulted in cure, and 19 in death. In 22 cases the method of operation is not mentioned, and of these 7 resulted in cure, and 15 in death.

[2] Zeitschrift f. Ohrenheilkunde, 1903, p. 354.

These reports are fairly accurate, although in some cases in which the operator opened first through the tegmen and then, later, extended the operative opening to the squama, the case has been reported sometimes as "squama" and sometimes as cases opened through the "tegmen."

It would seem from this series of cases that the best results are obtained when the abscess can be drained through the tegmen. This undoubtedly depends upon the fact that when the abscess has been drained through the tegmen tympani the operator has been able to open the abscess along the avenue of infection. When this can be done—as has been pointed out by Macewen and Ballance—there is very little danger of secondary meningitis, and very little danger of hernia cerebri, because, as the result of the infectious process, the meninges become soldered together and the subdural space obliterated over a given area. If the incision through the dura and into the brain substance is made through the membranes which have thus become adherent, there is very little chance of secondary meningitis following. If, however, the abscess is opened through the healthy dura, there is great danger of secondary meningitis, which, in the majority of cases, proves fatal. In 3 of my own cases, not included in this series—in which recovery ensued as the result of operation—in 1 case only was the abscess drained primarily through the squama. In 2 other successful cases the combined method was used—that is, the tegmen tympani was removed and the opening enlarged upward and outward into the squama, thus securing more room. In 1 of these cases drainage was made directly along the course of the path of infection, and recovery followed. This patient was seen several years later, and was perfectly well. In a second patient operated upon by one of my assistants during my absence the same plan was followed, and although the dura did not seem to be diseased, the rapidity with which the patient recovered would seem to indicate that the subdural space must have been obliterated as the result of a previous inflammatory process. In 1 patient operated upon by myself, and who made a perfect recovery, drainage was instituted through the squama, and in this instance the membranes appeared perfectly healthy. There was quite a large hernia cerebri in this case, but it was finally overcome, and the patient made a complete recovery.

These statistics would go to show, therefore, that in cases of brain abscess the operator should first search carefully for the path of infection through the tegmen tympani and tegmen antri, and if such a path is found the diseased bone should be removed. If more space is needed the opening may be enlarged upward and outward through the squamous plate of the temporal bone. In incising the dura this incision should be made through the diseased dura, if possible, as here the membranes will have become adherent. In the absence of any evidence of caries or necrosis of the tegmen tympani or

tegmen ant i, the bone should first be removed here and the dura exposed, as we may find diseased dura underlying apparently healthy bone. Our statistics also show that, in the majority of cases of temporosphenoidal abscess of otitic origin, the infection takes place in one or the other of these regions. The exploration should, therefore, begin here in every case. Such an exploratory opening, if more room is needed, may be enlarged upward and outward through the squamous plate of the temporal. Unless the symptoms are very urgent, I should be inclined, in future cases, in which the dura appears perfectly healthy, to adopt the suggestion of Mr. Ballance, and, after exposing the dura over a proper area, to incise this and pack the margins of the wound firmly with iodoform gauze, deferring an exploratory incision of the brain substance for from twelve to twenty-four hours. This procedure would serve to relieve the tension, while, at the same time, it would cause an amalgamation of the various layers of the membranes of the brain, thus obliterating the subdural space. Such a soldering together of the membranes would occur in the course of twelve to twenty-four hours. The brain substance could then probably be explored with comparative safety, and the abscess evacuated without much danger of secondary meningitis. When the condition admits of delay, I believe that this plan of procedure will be the proper one to follow.

The various methods of securing drainage in a brain abscess have been discussed so many times that it is quite unnecessary to review them here.

In appending the following bibliography of cerebellar and cerebral abscess, I wish to acknowledge my indebtedness to my assistant, Dr. Charles E. Perkins, who has so carefully collated these cases for me. His painstaking tabulation of symptoms has made the above review of this number of cases possible.

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ACTINOMYCOSIS OF THE SKIN OF THE FOOT.

By Leo Buerger, A.M., M.D.,
SURGEON TO THE GOOD SAMARITAN DISPENSARY; ASSISTANT IN PATHOLOGY, MT. SINAI HOSPITAL, NEW YORK.

Primary invasion of the skin and subcutaneous tissues by Actinomyces bovis is of such rare occurrence that I deem it not unwise to add another instance of this affection to the very few that have already been recorded in the literature. If we glance at the statistics of those who have made a special study of this subject we find that the cases number less than 20, and a careful perusal of the histories makes it evident that even some of these may have been due to secondary rather than primary invasion of the skin. Illich[1] was able to find but 11 cases in his series of 421. In the 58 American cases collected by Ruhräh[2] there were but 3 of primary skin affection. In a total of 628 cases from all sources the same author reports a total of 16 of the skin. Von Baracz[3] does not mention its occurrence in his large personal collection of 60 cases.

Leser[4] was the first to arouse interest in this particular localization by the publication of 3 cases. From a careful clinical and microscopic study he was able to distinguish two general types, an ulcerating and a nodular form. The first he described as being characterized by the formation of granulation tissue, by necrosis, and by the production of ulcers. The second commences with the appearance of a nodular or papular eruption which has a tendency to peripheral extension and central cicatrization similar to that occurring in lupus vulgaris.

According to most of the observers the affected skin is bluish or has a violaceous tint. There is a formation of nodular protruberances which coalesce, break down in places, and finally perforate so as to form chronic sinuses or indolent ulcers. Leser calls particular attention to the absence of involvement of the regional lymphatic nodes, and considers this of diagnostic importance.

If we review the histories of a number of the reported cases we note, first, that many of them represent extensive lesions involving not only the skin, but the fascia, muscles, and even the bones, and second, that certain cases of cutaneous actinomycosis of the face may be secondary to buccal invasion of the organism. If we subtract these from the total number, but very few instances of true primary cutaneous involvement remain. For the sake of reference, I shall briefly summarize the important data belonging to the histories of most of the reported cases.

[1] Klinik. der Aktinomykose, Wien., 1892.
[2] Annals of Surg., 1899, xxx, p. 417.
[3] Ibid., 1903, xxxvii, p. 336.
[4] Archiv. f. Klin. Chir., xxxix, p. 722.

CASE I.—Bertha:[5] Male, aged sixty-six years; thrasher. A small nodule appeared on the dorsum of the right hand; gradual enlargement and conversion into an ulcer. After eight months the ulceration had extended over one-third of the back of the hand. The surface of the ulcer is nodular, in places covered with a thin, livid epidermis; there are a few sinuses. The process is limited to the skin and subcutaneous tissues. Treatment: excision of the ulcer. Cure.

CASE II.—Bertha: Male, aged forty-five years; laborer on farm. Sustained a wound on the ball of the thumb. Four weeks later there was considerable swelling in the neighborhood of the wound with reddening of the hand. In the course of the next month a number of pea-to-hazel-nut sized foci of pus developed. Treatment: excision of diseased skin; curetting of wound. Cure.

CASE III.—Dreyfus:[6] Male, aged ten years; worked on a farm. He has had a swelling of the left mammary region for about six months. Now spontaneous perforation has occurred and ulcers have formed. There is an area about the size of a palm, of infiltrated skin over the breast; there are three ulcers with grayish yellow, pale, sluggish granulations. Treatment: excision; improvement. The author calls it an ulcerating and fungoid type of lesion.

CASE IV.—Gross:[7] Female, aged twenty-seven years, very anemic and thin with a suppurative process at the angle of the jaw on the left side. There is a red indurated flat lesion resembling lupus of the skin. The diseased area was extirpated and the actinomyces demonstrated.

CASE V.—Köhler:[8] Male, aged fourteen years; peasant. There developed a painful swelling of the whole of the left leg. This became localized to the upper part of the tibia, broke down and perforated after a lapse of one and one-half months. In the neighborhood of the sinus nodular infiltrations of the skin made their appearance and rapidly become necrotic. Upon admission, some three months after the onset of the disease, there was a mass over the upper third of the tibia about the size of a hen's egg. At its lower pole there was an ulcer at the bottom of which the exposed bone could be seen. Treatment: excision of diseased portions, removal of exposed bone. The inner tuberosity of the tibia was filled with a soft tissue in which numerous colonies of actinomyces were found. Improved, but not wholly cured two years after operation.

CASE VI.—Leser: Male, aged thirty-five years; merchant. Disease began with the formation of an inflammatory swelling a little below the middle of the back of the left forearm; ulceration of the skin then occurred; edges partly undermined, irregular, hard, surrounded by a ring of induration. Similar lesions were found in

[5] Wien. med. Woch., 1888, xxxv.
[6] Münch. med. Woch., 1903, I, p. 2291.
[7] Soc. de méd. de Nancy, 1896 (cited by Poncet).
[8] Charité Annalen. 1887, xii.

the following places upon admission to the clinic: (1) An ulcer on the right side of the head, almost the size of a silver dollar; (2) a lesion closely resembling that of lupus in the right infraclavicular fossa where there was an indurated area of skin presenting about a dozen lentil-sized, red-brown nodules; and (3) on the left side of the abdomen an ulcer similar to the one on the arm. Treatment: curettement, cauterization, excision. Cure.

CASE VII.—Leser: Male, aged thirty-four years; merchant. For the past six days he has had a swelling of the skin of the right calf. Three days ago chills and headache. Fluctuation easily detected, no involvement of lymph nodes. Incision, drainage, later removal of portion of underlying muscle. Cure after four months.

CASE VIII.—Leser: Male, aged twenty-nine years; locksmith. In the neighborhood of a recently-healed burn on the upper part of the right leg there developed a painful swelling of the skin with several purulent areas. Ulceration soon occurred. Two such areas were separated by indurated, undermined skin. Upon curetting the ulcers an indurated process was found to extend deep down into the fascia. Treatment: excision of diseased areas; cautery. Cure.

CASE IX.—Lührs:[9] Male, aged thirty-seven years. A hard tumor on the outer side of the popliteal region. Incision and evacuation of serous fluid, granulation tissue, and "sulphur" granules. Treatment: incision; drainage. Cure.

CASE X.—Lührs: Male, aged fifty years; laborer on farm. Behind the left sternocleidomastoid there is a hard, painless nodule which upon incision showed the typical actinomycotic granules. Treatment: incision. Cure.

CASE XI.—Milian:[10] The history of this case is that given by Hudelo, Gaston, and Lebar, when they presented the patient to the French Society of Dermatology. Their diagnosis was tuberculosis. Milian, however, had seen the case almost two years before and by microscopic examination had established the diagnosis of actinomycosis.

Male, aged fifty years; porter. Onset of disease, twelve years ago. On the sole of the foot near the inner border there was a slightly painful nodule about the size of a lentil. This remained stationary for several years. Five years ago little nodules appeared along the inner border of the foot. These became softened and discharged thin pus. When seen by the authors the following condition was noted: The skin over the inner surface of the foot was bluish, beset with nodules of a violaceous tint, some hard, others soft and closely resembling angiomas. Some of these had evidently broken down. Microscopic examination threw no light upon the nature of the process.

[9] Inaug. Diss., Göttingen, 1889.

[10] Bull. soc. franc. de dermat., 1905, xv.

CASE XII.—Monestie:[11] Female, aged thirty-six years. When seen by the author the patient had a tumor of the right submaxillary region. Seven months previously the disease began with a little nodule in the skin which gradually increased in size. After a period of four weeks the tumor ulcerated and evacuated some blood. Ever since there were intermittent discharges of pus and blood. At the time of examination she had an elongated, dark-red, or violaceous tumefied area in the skin, which showed areas of softening. About this there was a zone of induration. The teeth and jaws were healthy.

CASE XIII.—Müller:[12] Female, aged twenty-eight years. Two years previously patient had run a wooden splinter into the palm of her right hand near the base of the middle finger. The splinter healed in leaving a painless nodule. This became suddenly reddened without apparent reason. Incision revealed a cavity filled with granulations and a small splinter which was overgrown with actinomyces colonies. Cure.

CASE XIV.—Nocard and Lucet:[13] Male. Following the kick of a horse an abscess developed in the upper part of the left thigh. Perforating sinuses remained.

CASE XV.—Partsch:[14] Male, aged sixty years. Two months after the removal of a carcinoma of the breast two sinuses formed together with purulent areas in the scar. A small hazelnut-sized cavity filled with granulation tissue was found in the old scar. In this the actinomyces were demonstrated. The infection probably occurred at the operation. Treatment: curettage; excision of scar tissue. Cure.

CASE XVI.—Poncet:[15] Female, aged thirty-two years, was seen for an affection of the left cheek which had lasted four months. She first noticed a little nodule just below the angle of the mouth. The skin over it became red and then ulcerated. In spite of the extraction of a premolar which was supposed to have caused the lesion, a number of similar nodules appeared in the vicinity. At the end of three months the deeper parts became infiltrated, there was marked trismus and œdema extending into the parotid region. The cutaneous lesions at the time of admission to the hospital about four months after the beginning of the disease, are thus described: "toute la région comprise entre la commissure labiale et l'oreille, est recouverte d'élevures hémisphériques confluentes de 1 á 3 centimètres de diamètre, de 1 centimètre de hauteur. Leur sommet présente des cratères qui laissent échapper du pus contenant des grains jaunes actinomycosiques. La peau, á leur niveau, a une coloration rouge muqueux."

CASE XVII.—Tusini:[16] Female, aged thirty-four years. At the age of ten she sustained a slight wound of the left leg with a pitch-

[11] Thèse Paris, 1895, (cited by Poncet).
[12] Beitr. z. klin. Chir., 1888, iii, p. 355.
[13] Acad. de méd., 1888 (cited by Poncet).
[14] Breslauer aerst. Zeit., 1881.
[15] Deut. Zeit. f. Chir., 1886, xxiii, p. 497.
[16] Arch. f. klin. Chir., lxii.

fork. The wound healed and left a small scar. Ten years ago a few nodules appeared in the old scar. These grew gradually and discharged pus, leaving ulcers which slowly healed. Fresh nodules were repeatedly formed in the vicinity, spreading gradually over a large area until finally the whole of the left leg was involved. At the time of examination of the patient, Tusini found 43 ulcers and numerous sinuses. Some of these could be traced down as far as bone. The muscles of the leg were almost completely converted into fibrous tissue.

These 17 cases have been either reported or cited as being instances of primary actinomycosis of the skin. However, it will be seen at once that those recorded by Poncet, Monestié, and Gross, although they first showed lesions in the skin, could, according to their situation, have been secondary to infection by way of the mouth. It is indeed difficult to determine whether we are dealing with a primary skin lesion in the cases that occur in the cervicofacial region. And thus the old term "Actinomycosis cutis faciei" has justly fallen into disuse because of this very fact. The cases published by Köhler, Nocard, Lucet, Müller, and the first one of Lührs were evidently more deeply-seated affections, but caused by infection through the skin. If we are to include such examples as that cited by Müller (foreign body under the skin) under the actinomycotic lesions of the skin we would have to add the more recently reported instances of panaritium due to the same cause.[17] This leaves then but a very few cases, those of Bertha, Dreyfus, Milian, Partsch, Leser, and Lührs in which a primary actinomycosis of the skin was the main lesion.

The striking point noted by many of the observers is the resemblance of the skin lesion to some form of tuberculosis. Leser was the first to call attention to this and showed the importance of a thorough microscopic study. In the case in which Milian made the diagnosis we have another example of the difficulty in recognizing the disease. Hudelo[18] as well as most of the members of the French Society for Dermatology at a meeting of which the patient was shown, looked upon the case as most probably tuberculous.

In my own patient the presumptive diagnosis of an inoculation tuberculosis was made. The patient was a young girl who came to the Good Samaritan Dispensary complaining of a "wound" on her foot behind the toes.

S. B., Russian; female, aged sixteen years; operator, consulted me at the dispensary on March 4, 1907. Four months previously she noticed a tiny "pimple" on the back of her foot just behind the fourth toe. She does not remember having injured or wounded her skin in any way. She has lived in this country for eight years and always in New York City. The small red spot gradually enlarged until it

[17] Thevenot, Massaglio and Dor.

[18] Bull. soc. franc. de dermat., 1904, p. 358.

attained its present size. It causes her little pain, but considerable discomfort owing to the pressure of her shoetops. She has always been perfectly well.

The patient is a well-nourished, somewhat undersized but well-developed girl. Lungs, heart, and abdomen are negative. On the dorsum of the left foot just behind the interval between the third and fourth toes there is an irregularly elliptical tumefied area in the skin, 2.5 x 1.3 cm. (see figure). The skin is elevated about 4 mm. reddish-blue or violaceous in color, the epidermis intact but apparently thinned, particularly in several places where there seems to be a tendency to perforation. The whole area is soft to the touch and semifluctuating, its margins rise fairly abruptly and are surrounded by a slightly indurated zone. The general appearance is not very unlike an infected angioma. The femoral and inguinal glands are not enlarged.

Actinomycosis of the skin of the foot.

The area was circumscribed under cocain anesthesia, sliced off, and the base thoroughly curetted. The latter was found to be hard, apparently made up of dense connective tissue. Upon removal, a few drops of bloody pus were seen to come from the deep parts of the tissue. A number of fresh cuts were made through the lesion but nothing suggestive of sulphur granules was detected. The small number of actinomyces colonies (three in all of the tissue examined) explains the fact that they were overlooked.

Practically all of the diseased tissue was divided into pieces and examined. Twelve blocks were made and in only one of these were the actinomyces found. The general picture is that of a pro-

ductive inflammatory process with areas of purulent infiltration in the neighborhood of the parasites. Save for the epidermis which is intact over the greater part of the affected area, very little of normal corium or stratum subcutaneum is left. These are replaced by young connective tissue in various stages of development. The epidermis is thinned in places; here and there the stratum mucosum is invaded with leukocytes, shows necrosis and degeneration of the cells. The actinomyces colonies are but three in number. Two of these lie about 1 mm. below the surface, the third 1 mm. deeper. The threads stain well with the Gram method and the clubbed ends are well developed, staining intensely with acid fuchsin. Around each colony there is a zone of polynuclear leukocytes. The deeply-situated fungus is imbedded in rather old connective tissue.

A very striking feature is the large number of newly-formed blood-vessels. The connective-tissue cells or fibroblasts, are frequently arranged concentrically about these vessels for varying extents. Often these are succeeded by collections of plasma cells. These are very numerous and are to be seen not only in the vicinity of the vessels but scattered throughout the tisue. In the superficial layers there are many cells containing brown pigment granules. A few of these are to be seen scattered irregularly throughout. In general the connective tissue is very rich in cells. The sections made from the periphery of the lesion show connective tissue of an older type. Here the plasma cells and fibroblasts are few in number, the intercellular substance is in abundance and many elastic fibers are found.

There has been hemorrhage and necrosis in a number of areas. In one place there is a collection of giant cells grouped in a circular manner. Enclosed by them there are a few leukocytes and some hyaline spherical bodies which stain poorly with all the dyes. Whether these are remnants of some foreign body I was unable to prove with certainty. The presence of the giant cells, however, is suggestive.

During the first seven or eight days that the patient was under observation the granulations that had formed looked sluggish and unhealthy. The patient was given potassium iodide after the sixth day. In the second week there was marked improvement and after twenty-four days the wound was completely healed.

We were evidently dealing here with a case of primary actinomycosis of the skin, in which the history gave no clue as to source of the infection. Undoubtedly inoculation must have occurred at some point in the affected area. A careful search for a foreign body proved futile. Perhaps we may group this case under the type described as nodular, although no discrete nodules could be made out. However, the lesion may have been formed by coalescence of a number of smaller ones. The failure to ulcerate is an interesting feature when we consider that four months had elapsed since it was first observed, and the fact that this portion of the foot must have been

continually exposed to the pressure of the shoe. Finally, we may call attention to the small number of colonies. A superficial examination of but a few sections would have failed to reveal the true nature of the disease. Leser had made a similar observation in studying his own cases. In Milian's patient this same difficulty led to the probable diagnosis of tuberculosis. Perhaps a more thorough microscopic study of localized lesions of this type may cause us to change our present views as to the infrequency of actinomycosis of the skin.

HEMORRHAGES IN THE COURSE OF BRIGHT'S DISEASE, WITH ESPECIAL REFERENCE TO THE OCCURRENCE OF A HEMORRHAGIC DIATHESIS OF NEPHRITIC ORIGIN.[1]

By David Riesman, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE PHILADELPHIA POLYCLINIC AND COLLEGE FOR GRADUATES IN MEDICINE; ASSOCIATE IN MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; PHYSICIAN TO THE PHILADELPHIA GENERAL AND THE JEWISH HOSPITALS, PHILADELPHIA.

The occurrence of hemorrhage as a complication of Bright's disease has been familiar to clinicians since the days of Richard Bright (1827). But even before Bright, Latour,[2] in 1815, called attention to the coincidence of *epistaxis* and other forms of bleeding with dropsy, while the all-observing Morgagni, at a still earlier date, reported the case of a woman in whom, though she already had the odor of urine on her breath, vomiting of blood and bleeding from the nose proved beneficial. Rayer[3] was among the first to appreciate fully the significance of epistaxis as a symptom of Bright's disease. Naumann[4] cites the case of a young man who died in convulsions after having had repeated attacks of violent nose bleed, in one of which he lost as much as six pounds of blood. The autopsy showed enlarged and inflamed kidneys. While admitting that the hemorrhage in such cases might be purely accidental, Rayer was, nevertheless, of the opinion that it was more probably the result of an alteration of the blood, consequent upon the derangement of the urinary secretion.

The close connection between Bright's disease and *cerebral hemorrhage* was strikingly shown in the classical paper of W. Senhouse Kirk,[5] while ophthalmologists have made us familiar with the frequency of hemorrhage into the eye in the course of nephritis.

These various forms of hemorrhage have been attributed, particularly by Huchard,[6] to vascular degeneration and hypertension;

[1] Read at a meeting of the Association of American Physicians, Washington, D. C., May 7, 8 and 9, 1907.

[2] Quoted by Launois, Thèse de Paris.

[3] Traité des maladies des reins, i, 605.

[4] Quoted by Rayer.

[5] Medical Times and Gazette, xi, 515.

[6] Bull. et mem. Soc. méd. de hôp. de Paris, 1888, 3 s., v, 287–290.

but the interesting studies of Schoenemann[7] seem to demonstrate that, as far as nose bleed is concerned, these are not necessary factors. He found after death numerous superficial hemorrhages into the mucous membrane of the nose. The number of peripheral capillaries, that is, those near the epithelial surface, was increased; in many cases these capillaries had broken through the basal membrane, the capillary loops having forced their way through the basal epithelial cells. During life the capillary walls, as well as the epithelial covering, rupture, and the blood escapes upon the surface. Schoenemann did not observe these conditions in diseases other than nephritis. They cannot be regarded as the result of ordinary circulatory obstruction; the capillary walls themselves seemed normal in appearance, and the deeper vessels showed no degenerative changes, such as have been described in other parts of the body. Perhaps the changes are due to a circulating substance which penetrates by osmosis into the surrounding structures and weakens them and the capillary walls in such a way that they cannot resist the blood pressure.

That *metrorrhagia* may be a symptom of nephritis is not so well known, although several writers have called attention to it. Among the older authorities who mention it are Grainger Stewart,[8] and Lecorché.[9] Braun[10] reports 2 cases of metrorrhagia. Delbet[11] has recorded the case of a girl who died as the result of a profuse vaginal hemorrhage, in his opinion, dependent upon renal disease. Bonifas,[12] in an intractable case of uterine hemorrhage in a woman, aged fifty-five years, saw an arrest of the hemorrhage under antinephritic treatment. Quite recently, Violet[13] reported 3 cases of profuse metrorrhagia, apparently caused by interstitial nephritis. He points out, as does Cumston,[14] the importance of recognizing the connection between metrorrhagia and nephritis, as otherwise improper treatment may be instituted. Ergot, in the opinion of both writers, is contra-indicated in such cases.

Hemorrhage from the lungs, as a manifestation of renal disease, is rare. Cases are recorded by Hawkins,[15] Fisher,[16] and Duclos,[17] and the subject is mentioned by Dickinson, Fuerbringer,[18] and Senator.[19] In Hawkins' case, the hemoptysis continued for a year and two months, the autopsy showing cirrhosis of the kidneys. Accord-

[7] Arch. f. Laryng. und Rhin., 1901–2, xii, 437.
[8] Bright's Diseases, New York, 1871, 238.
[9] Traité de maladies des reins, 1875, 398.
[10] Quoted by Wieger (Launois, loc. cit.).
[11] Bull. soc. anat. de Paris, 1885, lx, 183–186.
[12] La normandie médicale, 1898, xiv, 102.
[13] Lyon médical, 1904, ciii, 428–438.
[14] Buffalo Medical Journal, 1904–1905, 718.
[15] Trans. Clin. Soc., London, 1891–2, xxv, 237–242.
[16] Bristol Med.-Chir., Jour., 1904, xxii, 234–247.
[17] Rev. gén. de clin. et de therap., 1890, iv, 329; 345.
[18] Die Krankheiten der Harn- und Geschlechts-Organe, Braunschweig, 1904, 132.
[19] Nothnagel's Encyclopedia of Practical Medicine, American edition, Diseases of the Kidneys, etc., 227.

ing to Duclos the hemoptysis, which is most frequent in old persons, is more often a precursor than an accompaniment of interstitial nephritis, and is due to sclerosis of the pulmonary vessels. The same cause that produces these changes in the vessels of the lungs also acts upon those of the kidneys, and thus brings about interstitial nephritis.

Fisher, in addition to 1 case of hemoptysis, reports 4 cases of *hematemesis* associated with small, white kidneys. In explanation of these hemorrhages, he propounds an ingenious hypothesis, to which I shall refer later. Another case of severe gastric hemorrhage, in a nephritic patient of thirty, is reported by Bonifas.[20]

Hematuria, a common symptom of acute nephritis, or of the acute exacerbation of chronic nephritis, may arise in the absence of acute manifestations, as in the cases reported by Askanazy[21] and Kusumoto,[22] in which the hemorrhage occurred apparently from the engorged veins of the renal pelvis.

An interesting form of nephritic hemorrhage is that into the *ear*, of which Schwartze[23] has reported a case. Haug,[24] in an exhaustive paper upon this subject, collects a number of cases from medical literature, all of them examples of hemorrhage into the structures of the ear in Bright's disease. Alibert, in 1880, devoted a thesis to the subject of otorrhagia in nephritis. Hemorrhage into the tympanic cavity may occur even before other symptoms of nephritis are manifest. It thus has the value of an early or prenephritic symptom.

I should not fail to mention the fact that Dieulafoy[25] believes that auditory disturbances, such as tinnitus, partial or complete deafness, and otitis media are more frequent in the course of Bright's disease than disturbances of the eye. Pissot[26] found among 66 cases of chronic nephritis, 34 suffering from auditory disorders.

In addition to the isolated hemorrhages I have so far described, we meet in Bright's disease, with a true *hemorrhagic diathesis*, 2 cases of which have come under my own observation. In a sense, the term hemorrhagic diathesis is also applicable to those cases of epistaxis, metrorrhagia, etc., in which the hemorr age is uncontrollable, and in which there is no local lesion to explain the bleeding.

Medical literature contains but few references to the hemorrhagic type of bleeding in its relation to Bright's disease. Avrad[27] saw a well-marked example in a case of scarlatinal nephritis. An incomplete report of a case was made by Imbert-Gourbeyer,[28] in 1856. Levi[29] reports 2 cases—1 of parenchymatous nephritis with epistaxis and hemoptysis, terminating in recovery; and 1

[20] Loc. cit.
[21] Zeit. f. klin. Med., Band lviii, 432.
[22] Deut. Archiv f. klin. Med., 1907, Band lxxxix, Heft 5 und 6, 405.
[23] Arch. f. Ohrenheilk, iv, 13.
[24] Deutsche med. Wochenschrift, 1896, 723.
[25] La France méd., 1877.
[26] Thèse de Paris, 1878.
[27] Gazette médicale, 1853.
[28] Quoted by Launois.
[29] Quoted by Launois.

of contracted kidney, with dropsy, hemoptysis, and epistaxis, ending in death.

Among systematic writers, Senator,[30] Fuerbringer,[31] Castaigne,[32] and Osler[33] mention hemorrhagic diathesis as a rare complication of nephritis. According to Wagner,[34] and to Senator,[35] the hemorrhagic diathesis sometimes precedes and is the cause of nephritis. More probably, however, the cause of the one is the cause of the other. A case of this nature is the one reported by George Johnson.[36] A man, aged thirty-seven years, was seized with epileptiform attacks, rigors, and pains in the limbs, followed by a purpuric eruption and general dropsy; the urine was albuminous, and contained epithelial casts and blood. Johnson believed that in this case, which terminated in recovery, the cutaneous eruption and the desquamative disease in the kidneys were primarily consequences of the poisoned state of the blood, and that the dropsy was a secondary result of the renal disease. A case analogous to Johnson's is reported by Girode.[37] Purpura hemorrhagica came on in the course of a chronic diffuse nephritis in an eight-year-old boy. The hemorrhages occurred very early in the disease, and suggested a common, infectious origin for both the purpura and the nephritis.

Samuel Gee[38] briefly mentions 3 interesting cases of purpura in children in association with nephritis. The onset was marked by diarrhœa, with blood in the stools; in 2 cases there was also vomiting. The purpura occurred in repeated accesses, but finally ceased, although the albuminuria persisted. These cases remind one of the erythema group so exhaustively described by Osler; in all probability they belong to it, and it is a fair assumption that the purpura, the diarrhœa, and the renal disturbances were all dependent upon one and the same infectious or toxic agent.

The history of the 2 cases that have come under my observation is as follows:

Case I.—J. S., male, aged thirty years, a Russian tailor, was admitted to the Polyclinic Hospital on March 21, 1904, in the service of my colleague, Dr. Schneidemann, with a severe inflammation of the eye. The patient, whose faimily history was negative, had had no other illness, aside from measles in infancy, except two previous attacks of nephritis: the first seven years before, characterized by swelling of the feet, and, the second, two years later, in which the face was chiefly swollen. The third had begun three weeks before, with swelling of the face; but he was able to work until a few days prior to his entrance into the hospital. When ad-

[30] Loc. cit.
[31] Loc. cit.
[32] Manuel des maladies des reins et des capsules surrenales, 1906, 268.
[33] Practice of Medicine, sixth edition, 669 and 743.
[34] Quoted by Senator.
[35] Loc. cit.
[36] Diseases of the Kidneys, London, 1852, 152.
[37] Arch. de physiol. norm. et path., 1887, 3 s., ix, 478–485.
[38] St. Bartholomew's Hospital Reports, 1880, xvi, 47.

mitted he was found to be pale and poorly nourished; the face was swollen, more particularly around the chin, the left eye, and the left malar and temporal regions. The left)eye was inflamed and reddened, and the conjunctiva chemotic. The right eye was painful on palpation, and its tension seemed increased. The heart was enlarged, the apex beat being in the sixth interspace in the nipple line; the first sound was muffled; the second much accentuated, with a tendency to reduplication; the radials and temporals were thickened. A blood examination showed: red blood corpuscles, 2,350,000; white blood corpuscles, 15,200; hemoglobin, 50 per cent., with a differential count as follows: polymorphonuclears, 78; small mononuclears, 13; large mononuclears, 4.5; eosinophiles, 3; transitionals, 1.5. There was no ascara; no ascites; no œdema of the legs; no enlargement of the spleen.

Dr. Schneidemann made a careful examination of the eye and reported as follows: "When the man came in he had redness and great œdema of both eyelids. Conjunctiva highly congested and chemotic; not tense, but relaxed and folded on itself. The lower conjunctiva was everted, and the upper slightly from the swelling; the motility of the eye was somewhat impaired, especially outward. The right pupil was moderately dilated, larger than the left, and immovable. Cornea was insensitive. Anterior chamber was extremely shallow. Iris nearly in contact with the cornea; tension + 2. A dull fundus reflex; but no details could be obtained. The œdema, mentioned above, extended to the region over the malar bone. On account of the man's condition, the functional testing of the eye for vision was unsatisfactory. There seemed to be some, but rather uncertain, perception for large objects. The patient complained of headache around the orbital, temporal, and malar regions."

On March 24 the patient began to bleed from the mouth, and, on examination, a carious tooth was found, which was thought to have caused a wound in the cheek; but, although the ragged edges of the tooth were broken off and styptic applications were made to the cheek, the bleeding continued. On account of the eye trouble, a leech was applied to the right temple; when it dropped off, there was free bleeding from the wound, a collodion dressing being required to check it.

On the 26th the patient had a convulsion, following which he was bled to the amount of fifteen ounces. After the venesection, he received an intravenous injection of 1200 c.c. of salt solution. Despite this, he had another convulsion on the same day.

On the 29th, a hemorrhagic suffusion appeared on the right side from the third rib to the costal margin, and a few purpuric spots were seen on the right arm. No history of an injury could be obtained, except the hypodermoclysis, which he had had three days before

On the same day he began to have hiccough, and gradually passed into a stuporous condition.

The ecchymosis on the right side became more extensive, and the spots on the right arm increased in number. Blood was running constantly from the mouth, and the breath was very fetid. The urine contained a large amount of albumin (1.5 parts in 1000), red blood corpuscles, and granular and hyaline casts.

On the 31st, a systolic murmur appeared, its area of maximum loudness in the third left interspace. Despite active treatment in the way of hot packs and stimulants, the pulse gradually grew weaker, and on April 1, eleven days after admission, the patient died. No autopsy could be obtained.

CASE II.—W. D., tavernkeeper, aged fifty-five years, born in Philadelphia, was admitted to the Jewish Hospital, September 2, 1904. He had never been ill, and denied drinking to excess. He attributed his trouble, namely, hemorrhages from the mouth and bowels, which had begun eight weeks before, to having neglected his own health in attending to his wife while she was suffering from an attack of pneumonia. When admitted to the hospital he was stuporous and delirious, and in evident uremia. The breath was urinous, and, according to the history obtained, he had voided no urine for forty-eight hours. The mucous membranes were pale; the tongue and teeth covered with recent blood clots; the heart sounds clear; pulse slow and feeble; pupils widely dilated. There was no ascites; no enlargement of the abdominal veins. The urine, which had to be drawn, had a specific gravity of from 1010 to 1012; contained albumin, and red and white corpuscles. Blood examination showed: red corpuscles, 4,440,000; white corpuscles, 6680; hemoglobin, 55 per cent.; differential count: polymorphonuclears, 83 per cent.; lymphocytes, 9.6 per cent.; mononuclears, 4.7 per cent.; eosinophiles, 0.6 per cent.; transitionals, 2 per cent.

The man died in a convulsion on September 10, 1904; the bleeding having continued to the end. There were no purpuric spots upon the surface. The autopsy revealed marked anthracosis of the lungs; a moderately enlarged heart without valvular lesion, and a smooth liver of normal size. The kidneys were enlarged and covered with small cysts; the capsule stripped with difficulty. On section, the kidney showed an almost total absence of cortical substance and marked fibrosis; the cut surface bled freely. The pathologist thought that the condition was one of acute exacerbation of a chronic, diffuse nephritis. The gastrointestinal tract and urinary bladder were normal.

There are four ways in which one may interpret the relation of the hemorrhagic diathesis to renal disease:

1. The hemorrhagic diathesis may be an accident; that is, an independent affection not causally related to the nephritis. This would obtain in such cases in which a septic infection, as, for in-

stance, ulcerative endocarditis, coexisted with the renal disease and caused the hemorrhagic state.

2. The hemorrhagic diathesis may be the cause of the nephritis. Cases of this type, as has been previously stated, have been observed by Wagner and Senator. It might be difficult, however, to prove in a given instance that the third explanation does not better apply.

3. The two may be due to the same cause. This relation of the two conditions is fairly clear in a number of cases in the literature, notably those of Johnson, Gee, and Girode, already cited.

4. The renal disease may be the cause of the hemorrhagic diathesis. This is the explanation I would give for my own cases, and is the group to which I especially desire to call attention.

The question arises, in what particular way does the nephritis cause the hemorrhagic diathesis? Several possible etiological factors suggest themselves: (1) Hypertension; (2) arterial disease; and (3) toxemia.

The first and second are important factors in the ordinary types of nephritic hemorrhage. In all probability they are a sine qua non; but they are not of themselves sufficient to cause a true hemorrhagic diathesis, for the production of which another element, presumably a toxin, is necessary. Flexner's[39] studies on the effects of snake venom have shown the existence of substances, by him termed hemorrhagins, that are capable of causing hemorrhagic extravasations through a destructive action upon the capillary endothelium. Toxins with analogous properties may, as Fisher[40] has suggested, be present in the blood in nephritis. The hypothetic poison, whatever it may be, in addition to acting upon the vessel walls, may also impair the integrity of the blood—an impairment similar to that found in chronic jaundice.

Quite recently, Friedeman[41] found in the pancreatic juice a powerful hemolysin possessing the property of dissolving homologous red corpuscles and causing hemorrhages. In health it is neutralized by a protective substance; but we may conceive conditions—among them Bright's disease—in which this substance fails to act. In its power to cause hemorrhage and paralysis, the poison of the pancreas resembles crotalus venom.

Prognostically, nephritic hemorrhages of every variety constitute a sinister omen; the hemorrhagic diathesis in particular seems to presage an early death. It is evident that in every obscure case of hemorrhagic diathesis, as well as in cases of apparently causeless bleeding from mucous surfaces, the possibility of a renal origin should be borne in mind.

CONCLUSIONS. 1. Bright's disease may cause hemorrhage from the nose, uterus, lungs, and stomach; hemorrhage into the brain,

[39] AMER. JOUR. MED. SCI., 1903, 202.
[40] Loc cit.
[41] Deutsche med. Wochenschr., 1907, Nr. 15.

eye, and ear; and also a more or less well-marked hemorrhagic diathesis.

2. The last-named condition is characterized by bleeding into the skin and from the mucous membranes.

3. The true cause of the hemorrhagic diathesis is unknown; but it is probably a toxin analogous to the hemorrhagins of snake venom.

4. In the other types of bleeding, arterial disease and hypertension are the chief factors.

5. The prognosis in all cases of nephritic hemorrhage is unfavorable, and generally hopeless when the hemorrhagic diathesis exists.

A CLINICAL STUDY OF FIVE HUNDRED CASES OF CONJUNCTIVITIS.[1]

By Hanford McKee, B.A., M.D.,

ASSISTANT SURGEON TO THE EYE AND EAR DEPARTMENT OF THE MONTREAL GENERAL HOSPITAL; OCULIST TO THE MONTREAL MATERNITY HOSPITAL, MONTREAL, CANADA.

(From the Pathological Laboratory of the Montreal General Hospital.)

Conjunctivitis in its different forms constitutes one of the commonest diseases we have to deal with in ophthalmic practice. Its frequency varies according to race, climate, and environment; but when one considers how exposed the conjunctiva, a mucous membrane, is to external influences and how subject to involvement in nasal and postnasal inflammations, an average of 30 per cent. of all ophthalmic cases does not seem high. Conjunctivitis, too, more than any other disease of the eye, is treated by the general practitioner. In many cases he must treat it, so that I have thought it not out of place to report the results and lessons from a systematic examination of a series of cases.

In diseases of the eye, as in affections of other parts of the body, we look to etiology before prescribing or giving a prognosis. Our latest text-books still say: "As regards their etiology, much has yet to be learned, although considerable progress has been made in this direction within the past few years." It is quite true that much has yet to be learned, but enough is known today to enable us, by a bacteriological examination of the mucous or mucopurulent discharge, an important symptom of conjunctivitis, to obtain knowledge of much value in these directions. By using bacteriological methods we come to divide cases of conjunctivitis, not from their clinical features into catarrhal, purulent, and membranous with their numerous subdivisions, but rather into two groups: (1) Con-

[1] Read at a meeting of the Montreal Medico-Chirurgical Society, June 7, 1907.

junctivitis with no known bacteriological cause, and (2) conjunctivitis in which there is a definite bacteriological factor.

The first group includes such causes as exposure to winds, irritant gases, dust, eye-strain, rhinitis, inflammation of the lacrymal sac, smoke, gouty diathesis, trichiasis, alcoholism, etc. The second group includes the pathogenic microörganisms of the conjunctival sac, which are not few in number.

The method of finding these microörganisms is simple and quite within the reach of all. It consists in making a smear from the conjunctival discharge, staining, and examining it. Further examination of the conjunctival discharge is made by the inoculation of suitable culture media. In making a smear preparation considerable care is needed in obtaining a small particle of conjunctival secretion. Often the patients constantly wipe their eyes, so that it is almost impossible to obtain enough secretion for examination. Again, many cases of catarrhal conjunctivitis do not at certain times show any discharge. In either case, with a small platinum loop one may "pick out" from the inner canthus a loopful of conjunctival secretion. When this is smeared well over a glass slide and properly stained and examined, pathogenic microörganisms will be found, if present. Gram's method is by far the most satisfactory stain. It eliminates at once the frequently present Gram-positive bacilli, which in many instances are non-pathogenic. There are many little variations in doing Gram's stain, but that which I have found satisfactory is the one followed in Axenfeld's clinic: (1) Aniline-gentian violet, 25 seconds; (2) wash with water; (3) Gram's iodine solution, 15 seconds; (4) wash with alcohol until no blue comes away; (5) wash with water; and (6) counterstain with safranin, 5 per cent. solution, 5 seconds. Having become proficient in the staining, it is next necessary to become acquainted with the various microörganisms met with in both the healthy and the diseased conjunctival sac.

A knowledge of the pathogenic microörganisms can be obtained only by seeing a large number of cases of conjunctivitis. While much satisfactory work can be done by a study of smear preparations, the real differentiation of the organisms must come from a study of their cultural characteristics—the especial difficulty of conjunctival bacteriology. The bacteria pathogenic for the conjunctival sac require special media in nearly every case. Even on special media the growths are usually sparse and likely to be overgrown by more easily cultivated organisms.

But what are the commonest pathogenic microörganisms met with in the different forms of conjunctivitis? In the Freiburg clinic, during 1902 to 1905 inclusive, 900 cases of acute and chronic conjunctivitis were examined, with the following results:

Morax-Axenfeld diplobacillus 519 cases; Koch-Weeks bacillus 41 cases; pneumococcus 34 cases; gonococcus 12 cases; Loeffler's

bacillus 6 cases; streptococcus 5 cases; Friedländer's bacillus 2 cases, and Pfeiffer's bacillus 3 cases.

Gonin, in the clinic at Lausanne, examined 310 cases of catarrhal conjunctivitis with the following results: Morax-Axenfeld diplobacillus 185 cases; Koch-Weeks bacillus 10 cases; pneumococcus 10 cases; streptococcus 5 cases, and staphylococcus 83 cases.

Pollock, of Glasgow, examined 361 cases of conjunctivitis with the following results: Koch-Weeks bacillus 189 cases; Morax-Axenfeld diplobacillus 62 cases; pneumococcus 9 cases; pneumococcus and diplobacilli 3 cases; gonococcus 17 cases; gonococcus and other organisms 3 cases; staphylococci and streptococci 15 cases; Koch-Weeks bacillus and Bacillus subtilis 1 case, and negative 62 cases.

Morax, of Paris, reports as follows: Koch-Weeks bacillus 175 cases; Morax-Axenfeld diplobacillus 258 cases; gonococcus 121 cases; pneumococcus 18 cases; influenza bacillus 6 cases; Loefler's bacillus 2 cases; staphylococci 6 cases, and unknown 10 cases.

Lundsgaard, of Copenhagen, examined 107 cases with the following results: Morax-Axenfeld diplobacillus 36 cases; pneumococcus 15 cases; gonococcus 5 cases; Koch-Weeks bacillus 3 cases; staphylococcus 5 cases; diphtheria bacillus 1 case, and Bacillus coli 1 case.

Bach and Neumann report on 110 cases as follows: Morax-Axenfeld diplobacillus 35 cases, pneumococcus 15 cases, and staphylococcus 53 cases.

Veasey in 64 cases of acute catarrhal conjunctivitis found the pneumococcus in 53 cases and the Koch-Weeks bacillus in 3 cases.

My report consists of a study of 500 cases, of which the results are as follows: Morax-Axenfeld diplobacillus 200 cases; pneumococcus 13 cases; gonococcus 10 cases; Koch-Weeks bacillus 7 cases; influenza bacillus 3 cases; meningococcus 1 case; McKee bacillus 9 cases; Micrococcus catarrhalis 12 cases; streptococcus 24 cases; staphylococcus 50 cases; Bacillus coli 5 cases; Bacillus xerosis, Bacillus Hoffman, and saprophytes 102 cases, and negative results 64 cases.

From these figures it will be seen that the most common forms are the Morax-Axenfeld, the Koch-Weeks, the gonococcic, and the pneumococcic conjunctivitis. It is an interesting fact that in different countries and localities different forms of conjunctivitis seem to predominate. In Nebraska and Washington pneumococcic conjunctivitis is the prevalent form; in New York Koch-Weeks is most frequently seen; while in Montreal by far the most common form is the Morax-Axenfeld.

In view of the impossibility of discussing the many interesting features of all forms, I have thought it best to consider a few of the commonest forms seen in Montreal, dwelling especially upon the two most important forms, the Morax-Axenfeld and the gonococcic

infections, and a third form of conjunctivitis which I believe has not yet been described.

Gonococcic Conjunctivitis. The position of the gonococcus in purulent ophthalmia unfortunately has not changed much. We all know too well what progress it makes if once allowed entrance to the conjunctival sac, and what efforts are needed to stay its course. While I have nothing new to offer on gonococcic infections, which seem as virulent today as ever, we have learned or are learning much about purulent ophthalmia, both in the infant and adult. Let me illustrate with some cases.

Case I.—*Ophthalmia neonatorum; typical history and clinical picture.* Smears from the conjunctival discharge showed numerous Gram-negative intracellular diplococci. This was thought to be an exceedingly virulent infection, but when the patient was brought back three days later the condition had almost entirely subsided. The inoculated tubes explained it. The organisms seen in the smear preparations were not gonococci, but Micrococcus catarrhalis or pseudogonococcus.

Case II.—*Ophthalmia neonatorum: typical history and clinical picture.* Repeated examination of the pus gave negative results. From cultures were obtained only a few colonies of the staphylococcus. The patient had been seen on Saturday, and when the mother returned the next Saturday she told me the baby's eyes had received no treatment since the Tuesday before.

Case III.—*Ophthalmia neonatorum: typical history and clinical picture.* From numerous smears made no microörganisms were found. Cultures, however, gave pure growths of the gonococcus. The case ran a stubborn course entirely different from Cases I and II.

Cases V, VI, VII were all purulent ophthalmias in adults. The clinical pictures were typically gonorrheal infections. The smears in each case showed the pus cells filled with Gram-negative diplococci. Tubes in each case showed the organisms to be the pseudogonococcus. The course in each case was mild, and of three or four days' duration.

The question of Gram-negative diplococci in the conjunctival sac is one to which I have given some thought. Why does one case of supposed gonorrheal ophthalmia run such a mild course and the next such a severe one, when from each Gram-negative diplococci are obtained? Different virulence of the gonococcus we say; granted, but also different microörganisms. I believe many cases of ophthalmia neonatorum and purulent conjunctivitis put down to gonococcic infection are not of that origin, but, as in the cases here cited, are due to other Gram-negative diplococci of much milder virulence.

Koch-Weeks Conjunctivitis. This is a form of conjunctivitis first reported by Weeks, in 1887, and since then reported almost

universally. The Koch-Weeks bacillus is now recognized as the most common cause of acute contagious conjunctivitis. This is a form which clinically may begin as an acute catarrhal conjunctivitis and run a mild course of a few days, or it may become very severe, with œdema of the bulbar conjunctiva and lids, and thick, purulent discharge. It attacks children and adults alike, tends to appear in the spring and fall of the year, and is one of the most contagious diseases we have to deal with. Happily complications seldom occur in this form; the most common are ulceration of the cornea and iritis. Pneumococcic conjunctivitis is a form which seems to favor northern climates, occurs especially in the winter, and is often associated with coryza. The clinical picture is a varying one from a mild catarrhal conjunctivitis to marked red-rose œdema, swelling of the lids, hemorrhages in the upper lid, and profuse discharge. It seems to attack children preferably, and is likely to be complicated by iritis, which may last longer than the conjunctivitis. Müller first described a bacillus which he found in cases of trachoma which he did not recognize as Bacillus influenzæ. Zur Nedden later reported cases of blennorrhœa neonatorum and other cases of acute conjunctivitis from which he isolated a bacillus which he called the pseudo-influenza bacillus. Numerous writers have reported influenzal conjunctivitis, an acute catarrhal conjunctivitis which may accompany systemic influenza.

Morax-Axenfeld's Conjunctivitis. The examination of two hundred cases of Morax-Axenfeld conjunctivitis here has brought out some interesting points, and what I have to say on this subject is based entirely upon the cases seen here. Described first by Morax and Axenfeld, and called by the latter because of its persistent qualities chronic diplobacillary conjunctivitis, this form has since been reported from many lands. Its presence in Canada was reported first in 1905 by me, and it has not as yet been reported here by any other writer. It is today one of the best known and most frequently seen diseases of the conjunctival sac. This form of conjunctivitis was first described as a chronic catarrhal conjunctivitis, which from the reddening seen at the outer and inner canthi was sometimes called angular conjunctivitis, and at times, from the associated blepharitis, blepharoconjunctivitis.

It is seen generally in one of four forms: (1) A mild catarrhal conjunctivitis with little or no involvement of the bulbar conjunctiva. (2) A catarrhal conjunctivitis with reddening at the outer and inner canthi. (3) A severe catarrhal conjunctivitis with marked involvement of the bulbar and palpebral conjunctiva and marked blepharitis. (4) An acute purulent conjunctivitis.

I have been struck with the number of acute cases that we have seen here—cases which clinically were Koch-Weeks or pneumococcic conjunctivitis, in which examination of the discharge showed them to be diplobacillary. Cases have also been seen in which

clinically the disease was follicular conjunctivitis, as well as other cases associated with trachoma and phlyctenular conjunctivitis. The cases associated with trachoma, contrary to the results of Myerhoff, did well on instillations of zinc sulphate. This, more than any other form of conjunctivitis, can be diagnosticated clinically; certain types are easily recognized, but on the other hand no form differs so much in its clinical appearance as does this. Morax-Axenfeld conjunctivitis differs here in many ways from the descriptions in the literature:

1. Many of these patients had severe subjective symptoms. They complained of pain in the eyes which was worse at night.
2. Many of the cases were acute, simulating blennorrhœa.
3. This form has been seen here very often during cold and wintry weather. I noted a number of times that after cold weather and snow a series of patients would present themselves at the clinic. The last time noted was April 10, the day after a snow-storm and wintry weather.
4. The cases associated with trachoma reacted well to the zinc sulphate.
5. Seven cases complicated with ulceration of the cornea were cured with instillations of zinc.
6. A series of cases of phlyctenular conjunctivitis in adults complicated by diplobacillary infections were seen.
7. Diplobacilli were found constantly in the noses of patients suffering from this form of conjunctivitis.
8. One patient, a boy was seen with excoriation about the nostrils; the examination of a little secretion showed the presence of diplobacilli.
9. In no case of diplobacillary conjunctivitis have I seen zinc sulphate fail. I have treated cases with silver nitrate and argyrol to no purpose. I have seen cases occurring in children return without improvement, but here the failure was not due to the zinc, but due to the inability to instil the drops. I have treated with argyrol or silver nitrate cases of trachoma in which diplobacilli were found in the conjunctival sac, but I never noticed any improvement in these cases until I began instilling zinc sulphate.

In addition to these we have seen a few cases that are of interest more from their rarity than from their practical value. During the past year we have had a number of cases of epidemic cerebrospinal meningitis. Conjunctivitis is a common complication of this disease. Of this number two cases had definite acute simple conjunctivitis. From Case I smears showed Gram-negative intracellular diplococci; cultures on hemoglobin agar gave a growth of Gram-negative diplococci, which were meningococci, that is, meningococcic conjunctivitis. Another case was one in which Petit's diplobacillus was present in the conjunctival sac. The conjunctiva had none of the clinical signs of diplobacillary infection. The

diplobacillus was differentiated from Morax-Axenfeld's by its cultural features. During the winter we had an epidemic of streptococcic conjunctivitis. The cases were all in infants. The clinical picture was one of pseudomembranous conjunctivitis. The infection was mild, reacting quickly to treatment. Another rare form seen was a case of lacrymal conjunctivitis of Parinaud. The patient, an adult male, came with a severe streptococcic conjunctivitis with severe pain in the eye, swelling of the lids, and involvement of the pre-auricular gland. The day following an iritis (absorption or toxin iritis) was present. The case ran a severe course

McKee Conjunctivitis. Upon April 6, 1907, a mother brought her infant of nine months to the Montreal General Hospital, and complained that the baby's eyes had been sore and running for five days. The clinical picture was as follows: Both eyes were involved. Upon the lashes was much dried secretion. The palpebral conjunctiva was intensely congested, while the bulbar conjunctiva was quite normal; the lids were not red or swollen. From the conjunctival sac there was a profuse mucopurulent discharge freely mixed with tears. A little of the discharge was smeared well over a glass slide, fixed, and stained. Upon examining the slide I saw here and there tiny Gram-negative bacilli which seemed too short and thick for the Koch-Weeks bacillus and too thick for Bacillus influenzæ. I had seen before this same bacillus, but in the hurry of a large outdoor clinic I had not pursued it farther, contenting myself with the thought that it was Bacillus influenzæ.

Tubes of blood serum, plain agar, bouillon, and hemoglobin agar were then inoculated and put in the incubator. After twenty-four hours a growth was seen upon the hemoglobin agar. The other tubes were negative. Smears showed this same small Gram-negative bacillus with the staphylococcus. The bacillus after a few days was obtained in pure culture, conjunctivitis set up, and from the conjunctival discharge this same small bacillus was obtained.

During a month nine such cases have presented themselves at the outdoor department. They have all been infants and all from among the Jewish colony here. They have all shown definite characteristic clinical features and from each case this same bacillus has been isolated.

Cultural Features. The tubes of hemoglobin agar inoculated with some of the conjunctival discharge gave a pretty and characteristic result which was constant in all the cases. After twenty-four hours in the incubator one sees over the surface numerous separate colonies of Staphylococcus albus.

Around each of these separate colonies radiating from them as centres are seen very fine, colorless, shiny, rounded colonies. These colonies are exceedingly fine, seem to keep separate, and extend over the whole surface. The original cultures from all the cases were as

the one described and showed how well this bacillus grows in commensal relationship with staphylococci. From the original tube the bacillus was obtained in pure culture by surface seeding a plate of hemoglobin agar. In trying to obtain it in pure culture by transferring from tube to tube the growths were always contaminated with staphylococcus. Over a plate of hemoglobin agar, however, by smearing a loop inoculated from one of the small colonies as far from the albus as possible, the bacillus in pure culture was readily obtained. The growth of the bacillus on hemoglobin agar is characteristic. The slant will be seen covered with a mass of tiny colonies. They remain separate and distinct, are colorless and, as will be seen from the tubes, the colonies are no larger than the sharp end of a pin; indeed the growth, though profuse, is at times exceedingly difficult to recognize. It is seen much better by artificial light than by daylight, especially with the proper reflection of light. The growth of the bacillus is very easily affected, even on hemoglobin agar, upon which it grows best. Upon freshly made hemoglobin agar it will not grow in less than forty-eight hours. The reaction of the media, too, is of the greatest importance. Hemoglobin agar neutral, 1 alkaline, 0.65 acid, 1 acid, and 1.75 acid to phenolphthalein was made up. Upon alkaline media it would not grow; upon the neutral and 0.65 acid it was transferable with great difficulty. The most satisfactory reaction and the one which has been latterly used is the 1 and 1.75 acid. The cultures on hemoglobin agar remain viable from two to three weeks, provided there is sufficient water of condensation in the tubes. One culture inoculated on April 11 was transferable on April 25, but not on May 3. It had not been kept in the cold nor had special care been taken of it.

For the human conjunctiva this bacillus is pathogenic. A conjunctival sac which was found to be free from microörganisms was well flushed out with warm water. Fifteen minutes later the sac was inoculated with a loopful of a twenty-four-hour growth. Twelve hours later there was a feeling of "something in the eye" and six hours later the eye showed a marked catarrhal conjunctivitis. The palpebral conjunctiva of the lower lid was especially congested. The posterior conjunctival vessels were somewhat dilated, otherwise the bulbar conjunctiva was not involved. From the mucopurulent discharge, which was here, too, freely mixed with tears, the organism was obtained.

With the washing from a slant on hemoglobin agar an ordinary house mouse was inoculated intraperitoneally. Eighteen hours later the mouse was unable to move and six hours later was dead. At autopsy the peritoneum was found injected and filled with a gelatinous, sticky exudate. Smears showed the pus cells filled with the bacilli, with little or no fibrin. Inoculations from the peritoneum on hemoglobin agar gave pure growths of the bacillus. This tube

was washed down and inoculated intraperitoneally into a white mouse, and twenty hours later the mouse was dead. Postmortem a marked peritonitis of the gelatinous type, similar to that of Case I, was found. From the peritoneum and from the heart's blood the bacillus was obtained in pure culture.

This microörganism, then, a cause of conjunctivitis, needs to be differentiated from the other known bacteriological causes of conjunctivitis. Differentiation from Morax-Axenfeld's diplobacillus, Petit's diplobacillus, Friedländer's bacillus, Bacillus coli, and Bacillus subtilis may be dealt with in a few words. It is far too different morphologically and culturally to necessitate going into minutiæ. The pathogenic microörganisms of the conjunctival sac from which it must be differentiated, however, are the Koch-Weeks bacillus and the different influenza bacilli, the influenza bacillus of Pfeiffer, the so-called influenza bacillus of conjunctivitis of Müller, and the pseudo-influenza bacillus of Zur Nedden.

1. *Clinical Considerations.* While the different bacteriological factors causing conjunctivitis do not always, yet in the majority of cases these organisms do, give rise to well-marked characteristic pictures. In Koch-Weeks conjunctivitis one finds reddened and œdematous lids, intense injection of the bulbar conjunctiva, with profuse mucopurulent discharge. In influenzal conjunctivitis there is a well-marked involvement of the bulbar conjunctiva and signs of influenza elsewhere. Bacillus influenzæ has been found in the normal conjunctival sac and in odd cases of conjunctivitis in which there were no general signs of influenza, but in the majority of cases influenzal conjunctivitis accompanies systemic influenza. Clinically, Koch-Weeks', influenzal, and the form of conjunctivitis set up by the bacillus here described, are very different.

2. *Morphology.* Differentiation by morphology is unsatisfactory and unnecessary. While the Koch-Weeks bacillus may be differentiated from Bacillus influenzæ by its appearance on the slide, and while the bacillus here described seems shorter and thicker than Bacillus influenzæ, I am ready to admit that morphologically they are strikingly similar.

3. *Cultural Features.* On media these organisms differ widely. The Koch-Weeks bacillus does not grow well on hemoglobin agar, as here used. It grows best on hydrocele or ascitic agar; when growing with Bacillus xerosis it is hardly perceptible and dies out very quickly in forty-eight hours or a little longer. Bacillus influenzæ in the presence of hemoglobin, after twenty-four hours, shows a profuse raised growth of round, whitish colonies. The growth is easily seen, the colonies being the size of an ordinary pinhead; older colonies show some change in color. The bacillus here described, on hemoglobin-agar gives a very characteristic appearance. Over the surface of the agar, with a proper reflection of light is seen a mass of tiny, pinpoint, colorless colonies. The growth is not easily

seen. This organism has also been cultivated on media free from hemoglobin.

4. *Pathogenicity.* The Koch-Weeks bacillus, while pathogenic for the human conjunctival sac, is not pathogenic for animals. Bacillus influenzæ is slightly pathogenic for some animals. Pfeiffer found, by injecting Bacillus influenzæ intravenously into rabbits, that a characteristic effect was produced. He attributed the results to toxic products present in the culture. In none of his experiments was he able to obtain effects resembling septicemic infection. Cantani by injecting Bacillus influenzæ into the anterior portion of the brain of rabbits succeeded in producing an acute encephalitis; the bacilli, however, were never found in the blood or other organs. This bacillus is pathogenic for mice. In every case in which it was injected intraperitoneally marked peritonitis was set up, and a septicemia, as evidenced by pure cultures of the bacillus being obtained from the heart's blood, resulted. This organism then is similar to the different influenza bacilli in morphology and in its growing well in commensal relationship with the staphylococcus. It is not Bacillus influenzæ for the following reasons: (1) The form of conjunctivitis set up differs from influenzal conjuncivitis. (2) This bacillus on hemoglobin agar differs widely from Bacillus influenzæ. On this media under most favorable conditions the growth is hardly perceptible and differs from Bacillus influenzæ on the same media, in size, color, and appearance. (3) This bacillus has been cultivated on media free from hemoglobin. (4) It is viable for a much longer period than Bacillus influenzæ. (5) It is pathogenic for the human conjunctiva.

We have then to deal with a new form of conjunctivitis set up by a new etiological factor. That factor resembles somewhat the bacillus of influenza, but differs from it widely on media, viability, and pathogenicity. In the examination of these five hundred cases of conjunctivitis, this series occurring within a month seems to be different from previously described types. Nine cases constitute a small number from which to draw conclusions, but the characteristic clinical features of these cases, caused by a microörganism not as yet described as a pathological factor in conjunctivitis, leads me to the conclusion that we have here to deal with a new form of conjunctivitis set up by a new microörganism of the conjunctival sac.

Until the clinical features of this disease from which the bacillus should take its name are better understood, I shall call it Bacillus McKee.

Treatment. Bacteriological methods, since they reveal to us the cause of conjunctivitis, also suggest the treatment. In mild cases of catarrhal conjunctivitis in which no microörganisms are found, the refraction and muscular balance of the eyes should be examined, nasal diseases should be attended to, and when there is any indication for it systemic treatment should be instituted.

Koch-Weeks conjunctivitis calls for preventive measures, the isolation of the patient, and, if the epidemic is a large one, closing of schools and such institutions. For Koch-Weeks conjunctivitis the application of the silver preparations has been the most satisfactory. Morax noted a great diminution in the number of bacilli after the application of silver nitrate. With this, cold compresses are found very beneficial. When there is any tendency to ulceration of the cornea or iritis, preventive measures need to be adopted immediately. Pneumococcic conjunctivitis, which is usually accompanied by severe swelling of the lids, is best treated with cold compresses and one of the silver preparations.

In gonococcic ophthalmia silver nitrate has been used extensively. Personally I prefer argyrol. In a limited number of cases I have never seen it fail.

In Morax-Axenfeld conjunctivitis we have in zinc sulphate a specific. Many cases which present the classical clinical features of Morax-Axenfeld blepharoconjunctivitis will be found to be not due to that microörganism, but to errors of refraction or other causes.

Bacteriological methods will never excuse one for neglecting such etiological factors as these, which should ever be borne in mind. Constant reference of these factors with no attempt at bacteriological methods is equally as inexcusable. Cases of acute catarrhal conjunctivitis occurring in children, especially in the spring, are probably not due to rhinitis, and while referring cases to the rhinologist is by no means to be discredited, certainly it is not the first procedure in such cases. Cases of one-sided conjunctivitis associated with some lacrymal disturbance due primarily to nasal affections are different, and here of course nasal treatment is the first indication.

Some Clinical Considerations. The scientific value of conjunctival bacteriology is acknowledged, but the practical value of this proceeding has not been given the position which it merits. This work is especially useful to the clinician, because so much of it can be done along with his clinical work in his office. These methods teach us that one must not put down all cases of acute simple conjunctivitis to Koch-Weeks infection, all cases of chronic catarrhal conjunctivitis to Morax-Axenfeld's diplobacillus, membranous and pseudomembranous forms to the diphtheria bacillus, and all purulent cases to gonococcic infection. In acute simple conjunctivitis we may find many other organisms present, in chronic catarrhal conjunctivitis none at all, in purulent ophthalmia many others than the gonococcus; indeed, the gonococcus is only one of eight or ten Gram-negative diplococci which have been found in diseased conditions of the conjunctival sac.

All these forms may be very similar in clinical features. The different bacteria cause at times definite characteristic forms of conjunctivitis, but at other times the clinical pictures give one no knowl-

edge of the etiological factors, so that the definite diagnosis depends upon the microscopic examination.

Bacteriological methods are of great assistance in different ways. Many cases of conjunctivitis are thus rapidly diagnosticated. We see many cases of trachoma which have received treatment for some weeks elsewhere. The similarity in their clinical picture to diplobacillary conjunctivitis would surprise one, the reddening at the outer and the inner canthi being at times marked. The presence of diplobacilli in the smear preparation settles the diagnosis at once. Negative results assist in excluding other forms of conjunctivitis and coming to the diagnosis of trachoma. The value of this knowledge will be better appreciated when one tries to cure trachoma with zinc, and diplobacillery conjunctivitis with silver. The results in the one case will be as unsatisfactory as in the other.

In ophthalmia neonatorum the knowledge that one is dealing with Bacillus coli or Micrococcus catarrhalis rather than with the virulent gonococcus or pneumococcus or the easily handled Morax-Axenfeld diplobacillus is of the greatest service. In purulent conjunctivitis it is important to know which of these many organisms is active. All this knowledge is of importance because when one has the gonococcus to deal with he knows he has a severe infection, but when the purulent ophthalmia is not due to the gonococcus or the pneumococcus the disease will run a mild course. The Koch-Weeks or Morax-Axenfeld infections require different methods of treatment, as also do those cases in which the bacteriological examination is negative. Clinical conditions will not give one this knowledge; to get such specific information one must turn to bacteriological methods. I do not at all wish to go to extremes, or to put bacteriological methods and examinations before clinical work; far from it, since clinical work in conjunctivitis has gone on and could go on perhaps without bacteriology. But I wish to put bacteriological methods and clinical work together. Together they make the diagnosis easy and sure, and when one has diagnosticated he knows.

Koch-Weeks conjunctivitis is the most contagious disease we have to deal with in ophthalmic practice, a disease which spreads rapidly, increasing in severity as it goes. In gonococcic as in pneumococcic and streptococcic infections we have virulent organisms to deal with which require constant care on the surgeon's part, while in purulent conditions from such microörganisms as Bacillus coli, Micrococcus catarrhalis, or staphylococcus we have comparatively mild infections. In all these cases treatment and results vary as do the etiological factor. Diplobacillary infection is a form of conjunctivitis which with proper treatment is easily cured, but without which it is a disease most chronic and likely to be complicated with ulceration of the cornea—resembling in severity the pneumococcic ulcus serpens. Even in phlyctenular conjunctivitis, these

methods will repay one. In trachoma negative results have their value. In many other cases, too, negative results tell us to look to other factors in etiology and suggest other lines of treatment. In all these forms bacteriological methods give us our diagnosis and, by telling us which of these different factors we are dealing with, put preventive measures, treatment, and prognosis on a practical basis.

This is what bacteriology does for the clinician, not only in conjunctival but in corneal work as well; this is where bacteriological methods and clinical considerations meet. Can one doubt their practical value?

The hemoglobin agar and other special media were made under Dr. Duval's direction. In working out Bacillus McKee he assisted me in many ways. I take great pleasure in here recording my indebtedness and thanks.

THE OPSONIC INDEX IN ERYSIPELAS AND ITS RELATION TO TREATMENT BY INOCULATION OF KILLED STREPTOCOCCI.

By Edwin H. Schorer, M.D.,
of New York.

(From the Rockefeller Institute for Medical Research, New York.)

After the observations of Wright and Douglas had stimulated investigations of all diseases of infectious origin, Dr. James C. Ayer kindly placed at our disposal for the determination of opsonic indices and for vaccination all cases of erysipelas treated in the wards of Bellevue Hospital, from January 1 to February 15 of this year.

During this time about 100 cases of erysipelas were admitted. Many of these cases were not suitable for investigation, as the patients entered the hospital at a late stage of the disease, after desquamation had occurred, or after there was complication with other diseases. Those cases in which no definite diagnosis of erysipelas could be made out were not studied. Altogether, the opsonic index was studied in 36 patients, and 37 patients received one or more injections of killed cultures.

The etiology of erysipelas was well established by the work of Fehleisen, who regarded Streptococcus erysipelatos as the cause of the disease. It is probable that streptococci causing erysipelas do not differ from those causing wound infections, for erysipelas often follows wound infections—infections of the mouth and scarlet fever. Moreover, streptococci from erysipelas transferred to other individuals may cause puerperal fever and other infections. In our series, erysipelas frequently followed coryza and wound infections.

Streptococci were isolated from cases of cellulitis and from blebs upon the skin in cases of erysipelas. Although it is possible that infection with streptococci can be best treated with killed cultures isolated from the case in question, the same culture being used for the determination of the opsonic index, yet the course of the average case of erysipelas makes it impracticable to isolate cultures from every case of the disease and to make a vaccine for its treatment. In many cases no blebs are formed, and even if a bleb were artificially produced, the patient might have recovered before the culture could have been isolated and the vaccine made. Moreover, since most patients are admitted to the hospital during the acute or during the advanced stage of the disease, treatment to be of service must be administered without delay.

A uniform mixture of streptococci from 4 cases of erysipelas was used in determining opsonic indices and in making vaccines. One of these cultures came from a bleb present with facial erysipelas and another was obtained from the discharging ear of a patient with erysipelas of the ear and otitis media; the third culture was from a case of erysipelas affecting the leg, and a fourth was from a bleb with erysipelas of the face and scalp. All of these microorganisms had the same cultural characteristics, and grew in long chains in bouillon. They produced hemolysis, caused acid formation in milk, and did not ferment inulin.

Technique of Determining the Opsonic Index. One tube of each of the first two cultures and two tubes of each of the third and fourth cultures were incubated twenty-four hours on glycerin-glucose-agar, to which 20 per cent. of sterile sheep serum had been added. From 2 to 3 c.c. of sterile salt solution was used to prepare an emulsion from these six slant agar growths. The emulsion was put in a small test tube containing some sterile sea sand; the tube was sealed in the flame and kept during one and a half hours in the shaking machine. The sand and emulsion in the tube were centrifuged for one minute and the fluid was drawn off. In this way, short chains of from two to four cocci were uniformly obtained.

The serum used for control was a mixture from two healthy adults. Our leukocytic emulsion was obtained by drawing ten drops of blood into about 10 c.c. of 1.5 per cent. potassium citrate in normal salt solution. The mixture was centrifuged, and without further washing the leukocytes were drawn off.

The mixture of leukocytes, bacteria, and serum in capillary tubes was incubated in the opsonizer of Wright at 37° C. for twenty minutes. The slides were fixed with methyl alcohol and stained with Loeffler's methylene blue. The cocci in fifty definitely outlined and isolated polynuclear leukocytes along the upper and low borders of the spread were counted. The slides uniformly showed well-preserved leukocytes and the chains of cocci were well broken up.

This method of determining the opsonic index does not differ essentially from the one used by Wright and Douglas. A series of experiments was made to determine the accuracy of the method. In these tests, Staphylococcus aureus, of which suspensions are easily prepared, was used instead of Streptococcus erysipelatos. The attempt was made to determine (1) the limits of error when several specimens of serum are drawn almost simultaneously from the same individual, and (2) the variation of the opsonic power of healthy individuals.

I. Five specimens of the blood of a healthy adult were drawn from five fingers of the same hand. The leukocytes used for the determination were washed twice in 1.5 per cent. potassium citrate in normal salt solution.

TABLE I.

	1st 100 leukocytes counted.	2d 100 leukocytes counted.	Phagocytic index.
Specimen 1	166	196	1.810
" 2	176	183	1.795
" 3	198	199	1.985
" 4	185	175	1.800
" 5	230	190	2.100

II. A series of ten specimens of blood from ten healthy adults was studied to determine the variations in opsonic power in healthy individuals. The leukocytes were twice washed with 0.85 per cent. salt solution. The number of cocci taken up by one hundred polynuclear leukocytes was counted in two preparations separately incubated, and counted by two workers, A and B. The phagocytic indices are as follows:

TABLE II.

Source.	A	B
N.	9.48	7.63
J.	9.16	5.20
B.	8.75	6.80
McL.	7.27	4.37
Z.	6.63	5.12
C.	6.60	5.37
S.	5.89	4.82
O.	5.84	4.57
H.	5.49	6.03
Ns.	4.91	4.37

In the early observations of Wright and Douglas, the opsonic index was determined by comparing the serum to be tested with a mixture of several normal sera (pooled serum). This practice has been almost universally discarded, comparison being made with a single serum. The great error introduced by this method is shown by tables III and IV, which contain the indices obtained by using each serum for comparison with all of the others. Table III (Series A) shows that the normal opsonic index varies from 0.52 to 1.93, and in Table IV (Series B) it varies from 0.57 to 1.75.

TABLE III—A.

Denominator.	Numerator. I.	II.	III.	IV.	V.	VI.	VII.	VIII.	IX.	X.
I.	...	0.97	0.86	0.77	0.70	0.70	0.62	0.62	0.58	0.52
II.	1.03	...	0.89	0.79	0.72	0.72	0.64	0.64	0.60	0.52
III.	1.15	1.12	...	0.89	0.81	0.80	0.72	0.72	0.67	0.60
IV.	1.30	1.26	1.12	...	0.91	0.90	0.81	0.80	0.76	0 68
V.	1.42	1.38	1 23	1.10	...	1.00	0 89	0.88	0 83	0.74
VI.	1.42	1.39	1.23	1.10	1.03	...	0.89	0.88	0.83	0.74
VII.	1.61	1.56	1.38	1.23	1.13	1.12	...	0.99	0.93	0.83
VIII.	1.62	1.57	1.39	1.24	1.13	1,13	1.01	...	0.94	0.84
IX.	1.73	1.67	1.48	1.32	1.21	1.20	1.07	1.06	...	0.89
X.	1.93	1.87	1.66	1.48	1.33	1.32	1.20	1.19	1.10	...

TABLE IV—B.

Denominator.	Numerator. I.	III.	IX.	VI.	II.	V.	VII.	VIII.	X.	IV.
I.	...	0.89	0.79	0.70	0.68	0.67	0.63	0.60	0.57	0.57
III.	1 12	...	0.89	0.79	0.76	0.75	0.71	0.67	0.64	0.64
IX.	1.27	1.13	...	0.89	0.86	0.85	0.80	0.76	0.72	0.72
VI.	1.42	1.27	1.12	...	0.97	0.95	0.90	0.85	0.81	0.81
II.	1.47	1.31	1.14	1.02	...	0.98	0.93	0.88	0.84	0.84
V.	1.49	1.33	1.17	1.05	1.02	...	0.94	0.89	0.85	0.85
VII.	1.59	1.41	1.25	1.11	1.08	1.06	...	0.95	0.91	0.91
VIII.	1.67	1.49	1.21	1.18	1.14	1.12	1.05	...	0.96	0.96
X.	1.75	1.56	1.38	1.23	1.19	1.17	1,10	1.05	...	1.00
IV.	1.75	1.56	1.38	1.23	1.19	1,17	1.10	1.05	1.00	...

III. Blood was taken from five healthy individuals and a pool was made by mixing equal volumes of each of their sera. The phagocytic indices were determined in duplicate after separately incubating and counting the opsonic preparation, and an average of these determinations was compared with the phagocytic index obtained with the pooled serum. The phagocytic indices determined as the result of counting 100 polynuclear leukocytes in each preparation were as follows:

	Z.	N.	J.	McL.	S.	Pool.	Calculated average.
A	6.08	7.64	5.61	5.88	7.25	6.49	6.57
B	6.89	7.79	7.78	7.11	7.17	7.20	7.75

IV. This experiment was made with blood from five individuals, one of whom suffered with a streptococcic and staphylococcic infection, and another with a staphylococcic infection. A pool was made of the five sera and the phagocytic index determined by counting the cocci in 50 polynuclear leukocytes.

	B	C
1. Normal	2.72	3.004
2. Normal	2.24	3.160
3. Normal	3.06	3.960
4. Streptococcic and staphylococcic infections	2.08	3.100
5. Staphylococcus aureus infection	3.40	4.080
6. Pool of five sera	2.80	3.300
Calculated pool	2.70	3.460

It is evident that the method of determining the opsonic index usually employed is not accurate. There is not always agreement between results obtained by counting 100 and 200 polynuclear leukocytes on the same slide. When separate specimens of serum from the same individual are made, there is even greater error. When sera from different healthy individuals are tested by comparison with a single normal individual, such great error is introduced that the determination has little value. The preceding tests show, moreover, that comparison of the serum to be tested with a pooled serum decreases this range of error.

Observations upon the opsonic index were undertaken with the methods recommended by Wright and Douglas, and subsequently employed almost universally. The error introduced by comparison with a single serum was diminished by the use of a mixture of two normal sera. To further diminish the errors which occur with all determinations of the opsonic index, composite charts embodying a considerable number of observations have been prepared, when possible. The possible error introduced by collecting observations made upon a variety of cases, some of which were complicated by conditions other than erysipelas, is recognized.

Vaccine. Twenty-four-hour cultures of the same strains of streptococci used for testing the opsonic index were used to make the vaccine, which was standardized by estimating the number of cocci per cubic centimeter.

Opsonic Index in Erysipelas. Before determining the changes in opsonic index produced by vaccination, a number of unvaccinated cases were studied. The most instructive of these cases are the two which follow.

Case I.—S., a man, aged thirty-eight years, who had a migratory, recurrent erysipelas of the face, ears, scalp, and neck, was admitted to the hospital on the fourth day of his disease. When his face was involved, his index was 0.7; when it was desquamating, the index had risen to 1.3; when his face was again involved, seven days later, the index was 1.4; and when it was desquamating again, the index had dropped to 0.8. When his neck became involved,

one day after his face began to desquamate for the second time his index was 1.0; two days later, with an index of 1.1, his back became involved, and three days later, with an index of 3.2, his shoulders and neck were again involved, and two days later, with an index of 1.1, the back and shoulders began to desquamate. (Chart I.)

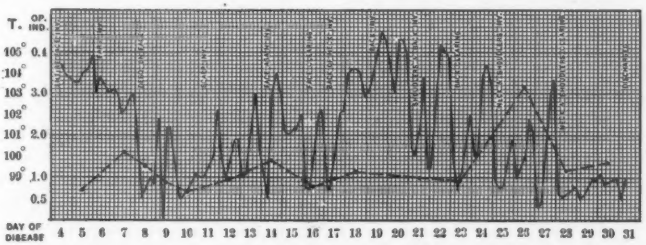

CHART I.—Temperature (unbroken line) and opsonic index (broken line) in a case of erysipelas (Case I).

CASE II.—A., a man, aged twenty-four years with erysipelas of the face and ears, was admitted on the eighth day of the disease with an index of 0.9. The next day his temperature dropped and desquamation began; his index was found to be 1.1. Subsequently the index, though the patient was perfectly well, remained below unity. (Chart II.)

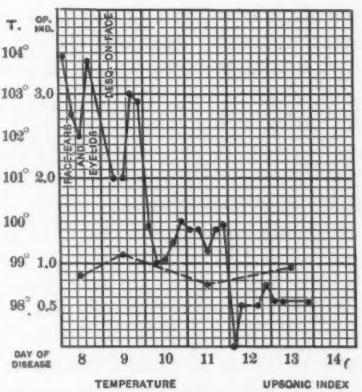

CHART II.—Temperature (unbroken line) and opsonic index (broken line) in a case of erysipelas (Case II).

In these two cases there has been no constant change of index corresponding with desquamation and recovery.

To further study the relation of the opsonic index to the course of the disease, the indices of all patients who had received no vaccine were tabulated (Table V) with regard to the day of the disease, and an average opsonic index for each day was determined.

TABLE V.

TABLE SHOWING THE OPSONIC INDEX AT THE TIME OF ADMISSION, BEFORE KILLED CULTURES WERE INJECTED, AND THE DAY OF THE DISEASE.

Day of disease.										
1	2	3	4	5	6	7	8	9	10	11
0.6	1.2	0.6	0.7	0.7	0.4	0.9	0.8	1.1	0.6	1.0
0.3	1.1	1.1	1.1	1.0		1.1	0.8	0.9		0.7
	1.0	2.4	1.4	0.9		0.6	1.3	1.7		1.0
		1.7	1.5	0.6		1.6				
			0.7	1.1						
			1.0							
			1.2							
0.45	1.1	1.45	1.1	0.86	0.4	1.05	0.96	1.23	0.6	0.9
Average.										

The composite chart indicates that erysipelas causes an increase of the opsonic index which reaches its maximum about the third day of the disease, and is followed by a gradual fall. The subsequent course of the chart represents, in very large part, observations made upon recurrent, migratory, and complicated cases. Ruediger[1] found that the index was high during an attack of erysipelas.

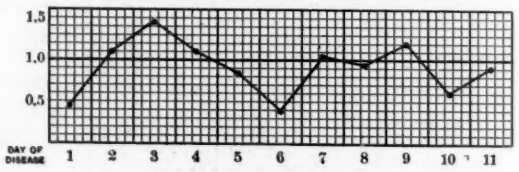

CHART III.—To show the average opsonic index and the day of disease before killed cultures of streptococci were injected.

RESULTS OF INJECTIONS OF KILLED CULTURES. During the investigation, 37 patients were injected with streptococci killed by heat. The number of cocci used for injection varied from 25,000,000 to 100,000,000. The effect on the opsonic index was studied in 10 patients receiving 25,000,000 cocci, in 5 patients receiving 50,000,000 cocci, and in 11 patients receiving 100,000,000 cocci. The results are indicated in the following tables with the opsonic index, before and after injection.

[1] Jour. Amer. Med. Assoc., 1906, xlvi, 108.

OPSONIC INDEX OF PATIENTS RECEIVING 25,000,000 STREPTOCOCCI.

	Before vac.	1 day after vac.	2	3	4	5	6	7	8	9	10
1	1.1	...	0.7	...	...	1.2	1.2	2.8			
2	1.0	3 0	2.1	1.7							
3	1.7	...	...	...	0.9	...	0.8				
4	0.6	...	...	1.5	...	0.7	4.1				
5	1.0	...	1.0	0.9	...	...	...	0.9		0.8	
6	0.7	...	1.3	...	0.9	1.1	...	1.0			
7	2.4	...	0.8	2.1	2.5	1.7					
8	1.2	...	1.3	1.0	...	1.1	1.7	1.1			
9	0.4	1.4	...	...	1.3	...	1.1	...	0.8		
10	0.3	1.1	...	1.7							
Aver.	1.04	1.83	1.2	1.48	1.4	1.16	1.78	1.45	0.8	0.8	

OPSONIC INDEX OF PATIENTS RECEIVING 50,000,000 COCCI.

1	1.0	0.8	...	0.8	...	...	...	...	0.7		
2	1.4	1.3	...	...	...	...	...	...	...	1.0	
3	0.8	1.4	1.2	...	0.8	...	1.2				
4	1.1	1.0	1.2	...	1.2	...	1.1	...	0.9		
5	0.6	0.4	...	1.0	...	1.1	...	1.0	0.9	...	1.1
Aver.	0.98	0.98	1.2	0.9	1.0	1.1	1.15	1.0	0.83	1.0	1.1

OPSONIC INDEX OP PATIENTS RECEIVING 100,000,000 COCCI.

1	1.2	...	...	0.5	...	0.5	...	1.3	0.5	0.6	0.8
2	1.0	1.0	...	0.9	...	0.8					
3	1.0	...	1.1	...	...	0.8	1.9				
4	1.1	0.3									
5	0.9	...	1.2	...	0.6	1.0	0.8				
6	1.0	0.8	1.3								
7	0.8	0.4	1.3	0.6	1.3	...	0.9				
8	0.8	...	1.2								
9	1.5	...	1.1	0.7							
10	0.6	...	1.0	1.0	0.9						
11	1.2	0 9	2.4	1.0	1.5	...	1.2	...	1.0		
Aver.	1.029	0.68	1.325	0.74	1.08	0.825	1.2	1.3	0.75	0.6	0.8

Some of the results of vaccination on the opsonic index are summarized in the following table:

	25,000,000.	50,000,000.	100,000,000.
Index rose without preceding fall	5	1	4
Index fell with subsequent rise	3	1	4
Index remained unchanged	1	2	1
Index fell and remained depressed	1	1	2

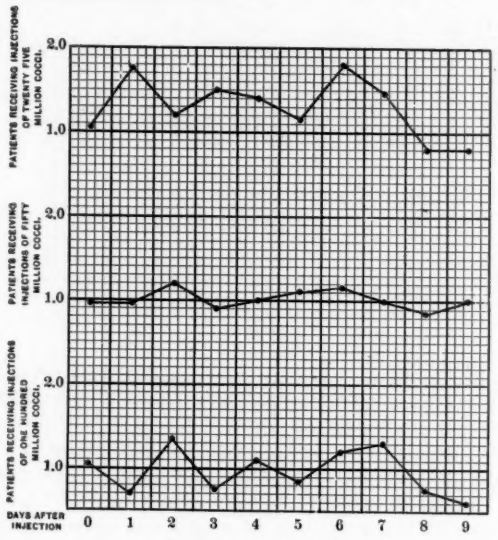
PATIENTS RECEIVING INJECTIONS OF TWENTY FIVE MILLION COCCI.
PATIENTS RECEIVING INJECTIONS OF FIFTY MILLION COCCI.
PATIENTS RECEIVING INJECTIONS OF ONE HUNDRED MILLION COCCI.
2.0
1.0
DAYS AFTER INJECTION
0 1 2 3 4 5 6 7 8 9

CHART IV.—To show the average effect of vaccination on the opsonic index

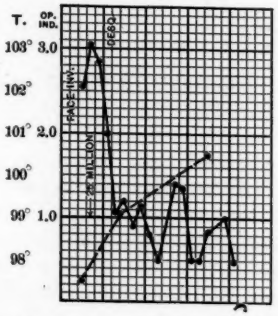

CHART V.—H., an adult male, had been suffering with coryza for about two weeks previous to admission. He had a chill on the day of admission and developed erysipelas of the face. He received one injection of 25,000,000 cocci on the first day of the disease. (Temperature, unbroken line; opsonic index, broken line).

The effect of vaccination on the opsonic index is represented by Chart IV, which shows the average of the opsonic indices for the different days after vaccination with 25,000,000, 50,000,000, and

100,000,000 cocci. Charts V, VI, and VII are from individual cases and show rise of opsonic index after injection of varying amounts of killed streptococci.

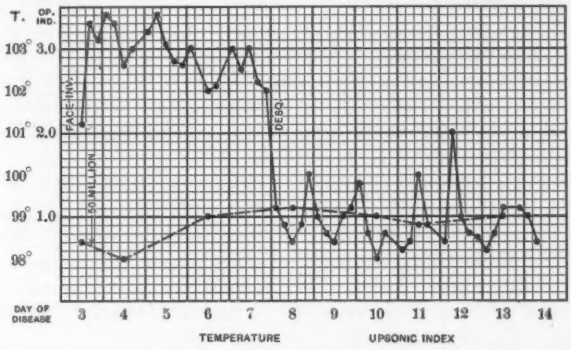

CHART VI.—C., an adult male, suffering with erysipelas of the face and delirium, received an injection of 50,000,000 cocci on the third day of the disease. (Temperature, unbroken line; opsonic index, broken line).

When 25,000,000 cocci are injected, not only is there no negative phase of the opsonic index, but the index is elevated after twenty-four hours. On the day after the first elevation, there is a fall, but the index maintains a level considerably above normal during seven

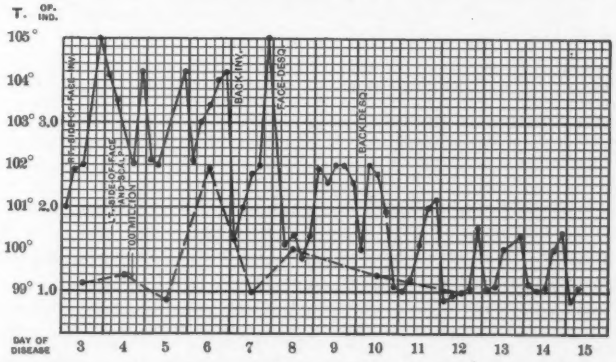

CHART VII.—M., a woman, twenty-three years old, was admitted on the third day of the disease with erysipelas of the right side of the face. Two days before admission she had had a severe chill, felt nauseated and weak. She received 100,000,000 killed cocci on the fourth day of the disease. (Temperature, unbroken line; opsonic index, broken line.

days. Only one-half of the patients discharged from the hospital as cured have a higher index on discharge than on admission.

The opsonic index determined with streptococci from patients with erysipelas shows no constant change at the time of desquamation. At the time of desquamation, the opsonic index was higher

than it had previously been in 8 of 13 cases, and twice it was lower than it had been at any time during the disease.

It is further of interest that of 33 patients whose indices were determined, the indices of 22 of them fell after desquamation. Of these, 2 have been again admitted to the hospital with recurrence.

Of 3 cases of recurrent erysipelas, in 2 there was a lower index at the time of desquamation than there had been before desquamation. One patient had a higher index at the time of the first desquamation and a lower one at the time of the second desquamation than had been observed in the case before.

Repeated Injections of Killed Streptococci. Several cases of migratory erysipelas and several with complications, such as otitis media and pyemia, received more than one injection of killed cultures. In these cases the first injection produced no marked increase of the opsonic index. The second injection was made after an interval of from three to ten days, and was usually smaller than the first. In most cases, the index ultimately rose.

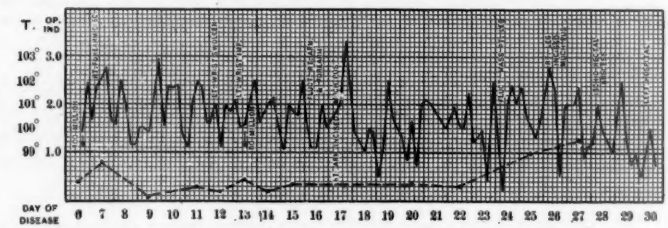

Chart VIII.—F., a woman, thirty-one years old. Five days before admission the patient's right arm began to swell and became red. She felt weak and feverish, and had numerous attacks of vomiting. There was no history of chill or trauma. This patient received an injection of 100,000,000 cocci on the sixth day of the disease, and 50,000,000 cocci on the thirteenth day of the disease. Complications were pyemia and apical tuberculosis. (Temperature, unbroken line; opsonic index, broken line).

In 4 injected patients whose opsonic index was determined at intervals, an intercurrent disease developed. Of these, 2 had pneumonia, 1 pyemia (Chart VIII), and 1 died with the diagnosis of tuberculosis and nephritis (Chart IX). In all of these patients the index rose with the development of the complication. The rise was especially marked with the appearance of pneumonia (Chart X). The significance of this cannot be determined, since only 1 patient with pneumonia died and no autopsy being made, the microorganism causing the pneumonia could not be determined.

Summary of Clinical Results. *Temperature.* In the first few hours following an injection of killed cultures, there may be a trivial rise of temperature from 0.2° to 0.6° F. There can be no definite conclusions as to the permanent effect on temperature.

Delirium. A large number of the injected patients, as well as those not injected, were delirious at times, so that a conclusion

regarding the relative frequency of delirium after injection is not possible.

Desquamation. Of 21 uncomplicated cases of erysipelas treated by the injection of killed cultures, injections were made twice on the

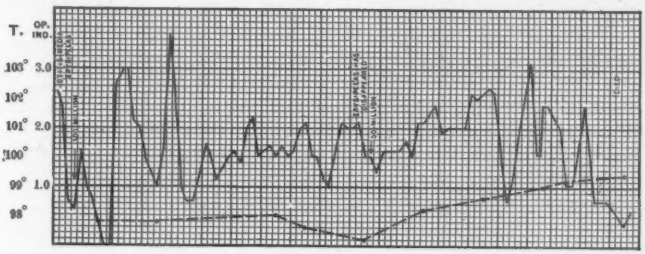

CHART IX.—H., a male, was admitted to the hospital December 3, 1906, with cystitis. On December 27 he developed otitis media, and on January 6 erysipelas of the face. Blood cultures were found to be negative. On January 10 he received 100,000,000 streptococci, again on January 16, 100,000,000, and on January 26, 50,000,000. He was never cured of his otitis media. He died February 5 with a diagnosis of apical tuberculosis and nephritis. (Temperature, unbroken line; opsonic index, broken line)

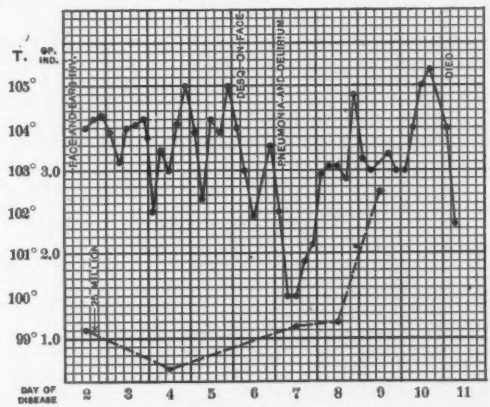

CHART X.—G., a man, thirty-four years old, was admitted on the second day of his disease. On the day before admission the patient had had a severe chill; his face began to burn and became red. He received 25,000,000 killed cocci on the day of admission; on the seventh day the disease was complicated by pneumonia. The patient died on the eleventh day. No autopsy was obtained. (Temperature, unbroken line; opsonic index, broken line).

first day of the disease; these patients desquamated on the second and seventh days, respectively. The average duration from onset to desquamation when treated by injections of antistreptococcic serum, as reported by Dr. Ayer,[2] in 1905, was seven and one-half days. Two cases of the present series were injected on the second

[2] Medical Record, 1905.

day of the disease and desquamated on the fourth and sixth days, respectively; an average of 10 cases injected with antistreptococcic serum on the second day by Dr. Ayer desquamated on the seventh day. Four cases injected with killed cultures on the third day of the disease desquamated on the fifth, fourth, fifth, and eighth days, respectively; an average of five and one-half days as compared to an average of six and nine-tenths days, as observed by Dr. Ayer in 21 cases receiving antistreptococcic serum on the third day. Six patients were injected on the fifth day and desquamated on the fifth, eighth, fifth, eighth, eighth, and tenth days of the disease. Two patients were injected on the fifth day of the disease and both desquamated on the seventh day. One patient was injected on the sixth day and desquamated on the seventh day. Three patients were injected on the seventh day and desquamated on the eighth, ninth, and tenth days, respectively. One patient injected on the ninth day of the disease desquamated on the eleventh.

The average duration of the disease in the 21 cases in this series is six and eight-tenth days. In 79 cases of erysipelas which received only local treatment, Dr. Ayer found the average duration of the disease to be nine and four-tenth days, which is two and eight-tenths longer than that of the present series. Of 48 patients receiving antistreptococcic serum, the average duration was found to be about the same as in this series.

The relation of dosage of streptococci to desquamation was as follows: Those receiving 25,000,000 cocci desquamated three days after injection; those receiving 50,000,000 cocci desquamated three and one-half days after injection; and those receiving 100,000,000 cocci desquamated two and four-tenths days after injection.

Migration. Migratory forms were found in 8 patients who had received injections of killed streptococci. Whether this migratory form was caused by injections of cultures cannot be determined, since other cases of the migratory type were observed when no injections were made. One of the injected patients with this form of the disease died; this patient had previously received 60 c.c. of of antistreptococcic serum and received one injection of killed cultures of streptococci three days before death. The disease, however, was complicated with chronic interstitial nephritis.

It is quite clear that injections of killed cultures of streptococci from erysipelatous lesions do not prevent migration, even if the opsonic index rises.

Recurrence. Recurrence was observed in a number of cases treated with injections of killed cultures. Since February 15 two of the patients included in this investigation have been again admitted because of recurrence. It is well known that an attack of erysipelas will not prevent a second attack of the disease, hence it is hardly to be expected that the injections of killed cultutes will prevent future attacks. Of the 37 patients who received injections

of killed cultures, 3 died. In all of these the erysipelas was complicated by some other disease.

The opsonic index is subject to such great irregularity that its determination gives little indication of the severity of the disease and is of no value for prognosis. There is in most cases of erysipelas an increase of the opsonic index occurring most often during the first three days, and this rise is followed by a fall. The injection of killed streptococci causes, on the whole, an increase of the opsonic index, but a relation between the elevation of the index and the improvement of the patient was not observable.

It is difficult to determine the value of the injection of killed cultures of streptococci in erysipelas. While this injection does not prevent migration and recurrence, the apparent shortening of the duration of the disease suggests that injections have some value. Yet the effect upon the duration of the disease is uncertain because during the time of our investigation no suitable cases remained untreated with which comparison could be made, and it is known that the duration of the disease varies in different years.

This investigation was made possible through the kindness of Dr. J. C. Ayer. I wish to express my obligation to Dr. Ayer and to Dr. Gordon Lindsay, the house officer in Bellevue Hospital.

REVIEWS.

PHYSICAL DIAGNOSIS, WITH CASE EXAMPLES OF THE INDUCTIVE METHOD. By HOWARD S. ANDERS, A.M., M.D., Assistant Professor of Physical Diagnosis in the Medico-Chirurgical College, Philadelphia. Pp. 456; 88 illustrations in the text, and 32 plates. New York and London: D. Appleton & Co., 1907.

DR. ANDERS desires to improve the student both in his technique and in his reasoning processes—two things in which, as he justly contends in the preface, the ordinary student is lamentably weak. He holds that the work of the diagnostician is akin to that of a detective, and he has attempted, therefore, to apply the principles of inductive reasoning to physical diagnosis. He limits physical diagnosis to those diseases of the chest and abdomen which can be detected "by the aid of signs denoting the abnormal physical condition of the organs or structures under examination." This excludes all those objective phenomena occurring in diseases of the nervous system, of the joints, muscles, etc., which, of course, should be regarded as physical signs.

As a whole, the book is very good. The style is clear, the arrangement logical, the illustrations fairly demonstrative. The majority of the latter are borrowed, although there are 11 original plates in the body of the book somewhat similar to those in Musser's work, and 21 plates showing a considerable number of Röntgengrams of the chest and abdomen, taken by Dr. Pfahler, which are excellent.

After a section devoted to topographical anatomy, Dr. Anders takes up inspection; but he fails to note that a normal thorax may co-exist with congenital anomalies of the lung and marked displacement of the heart. It is not clear why he says that rapidity of breathing is "not strictly a physical sign in itself." He recognizes pulsating empyema only on the left side, although it has been observed on the right. In the section on palpation he lays great stress upon the value of fremitus as a physical sign. He includes under this not merely the vibrations produced in the chest wall by the spoken voice, but all other vibrations, whether due to rales or friction, which may be felt by the hand applied to the body. The section on auscultatory percussion might have been somewhat fuller, and some of the factors causing inaccuracy should have been mentioned. It might be inferred that percussion over the ribs should be avoided.

The most unsatisfactory part of Dr. Ander's book is his discussion of the subject of pitch. This is partly to be explained by the fact that of all modifications of physical signs it is the one responsible for the greatest amount of confusion and difference of opinion. In the present work the confusion is by no means made clear. For instance, we have the sweeping statement that "pitch is the most important element in the differential diagnosis of air-less from air-containing tissues." Then, "the transition from clearness to dulness is realized more by the gradual elevation of pitch, than by any other acoustic attribute." On the next page we find "the louder or clearer the sound, the lower the pitch. The higher or shriller the sound, the less its loudness." But the student is cautioned "not to confuse the high-pitched, dull sound with the high-pitched tympanitic note." There is then a long discussion of the pitch of the percussion note over the lungs in normal and in morbid conditions, and particularly the modifying effect of tension, which does not serve to make the subject clearer; and in no place does Dr. Anders recognize what is rather the more common opinion of the present day, that pitch and loudness or intensity are essentially different factors, although, under certain circumstances, they may vary together. The eagerness to use pitch as an important element in physical diagnosis becomes almost absurd when it is applied to such a complex noise as the succession splash (p. 186), and its variation used for differentiation.

There is a seeming misstatement on page 13, that in retraction of the lungs, due to a pushed-up diaphragm, the borders of the lungs are motionless. The motion of the lower borders, under these circumstances, is one of the most trustworthy signs of differentiation from pneumothorax. Dr. Anders lays great stress upon auscultation directly, as well as with the stethoscope. He does not pay enough attention to the different kinds of information furnished by the different types of stethoscope, nor does he explain in sufficient detail the types of sound heard best with the ear, and those heard best by mediate auscultation. He believes that the transmission of the whispered voice is often more valuable than the transmission of the spoken voice. He does not differentiate very clearly between the different types of pectoriloquy, although he lays a good deal of stress upon the variations in the pitch.

In his discussion of physical diagnosis of the heart, it is necessary to take sharp issue with the statement that "when the alteration of the form of the precordium is more general, the prominence more marked, and unmistakable fulness of the intercostal spaces evident, it points to the presence of a pericardial effusion." Actual bulging of the precordium, involving the bony structures, as a result of pericardial effusion is extremely rare. Again, systolic retraction in the neighborhood of the nipple cannot be dismissed with the statement, "its significance is adhesive pericarditis," for it occurs in other

conditions. Hypoplasia of the lung is not mentioned as a cause of cardiac displacement.

Dr. Anders follows the prevailing view in preferring the deep to the superficial cardiac dulness. It is rather interesting to read the direction that, during the examination of the heart, "the patient should be at rest bodily, and serene in mind." On page 276 stress is laid upon the pitch of the second sound in contradistinction to its intensity. There is a very good, although brief, discussion of cardiac rhythm.

In the discussion of the various points relating to the physical signs of heart disease, it is necessary to begin by disputing vigorously the statement (page 287): "Given these two physical signs [area of greatest intensity and time of the murmur] in conjunction with the anatomical and physiological data related thereto, and the pathological significance is virtually a matter of logical deduction with syllogistic regularity." This may be compared with the more conservative statement of Fraentzel, who, in his later life, felt that after four or five hours devoted to the careful study of a case of heart disease, he could sometimes feel reasonably sure of the diagnosis.

In discussing the murmur of mitral stenosis no mention is made of the interrupted diastolic murmur, perhaps the most characteristic of all the varieties. The systolic murmur heard in the left axilla in mitral regurgitation is ascribed simply to the reflux of blood through the pulmonary veins. In aortic regurgitation no mention is made (excepting in one of the hypothetical cases on page 360) that in nearly all cases a systolic, as well as a diastolic, murmur is heard—a fact recognized by all the earlier writers, and to which Tyson, among the modern authorities, gives emphasis. In discussing tricuspid insufficiency no mention is made of pulsation of the liver as an important physical sign, though this is twice mentioned in connection with diseases of the liver. Among the rarer murmurs should have been mentioned the systolic vascular murmur that is sometimes heard in brain tumors, and in organic disease of the meninges and the skull.

The final section of the book is devoted to the examinations of the organs of the abdomen. Dr. Anders makes the original suggestion —at least it is new to us—of dividing the abdomen into six regions by lines radiating from the umbilicus. This seems, in all respects, a logical and practical method, and the best that has hitherto been suggested. Each of the six regions is in a sense an entity, containing organs that, clinically, are properly grouped together. The rest of this section, however, cannot be regarded as satisfactory. It is rather a catalogue of the various conditions that may occur, than a precise description of the physical signs which lead to their recognition. The ovarian cyst is not mentioned as one of the difficulties in the diagnosis of ascites. The interesting physical signs of subdiaphragmatic abscess and pyopneumothorax are not

even mentioned. The value of the study of the pulsation of the right common iliac artery in appendicitis is ignored. Retroperitoneal sarcoma is said to project in the right lower sextant.

In the diagnosis of the position of the stomach, numerous methods are altogether omitted, including auscultatory inflation introduced by Musser. In a discussion of the auscultation of the stomach and intestines the revolutionary work of Cannon has not been mentioned, and auscultation, a most valuable method, is dismissed with a brief paragraph commencing with the statement that it is of little diagnostic value. The value of the absence of liver dulness as an indication of pneumoperitoneum, is forgotten. The differential diagnosis of the different types of renal tumor is dismissed with a brief paragraph. The physical examination of the intestines occupies two and one-half pages, and is wholly inadequate.

A very successful effort has been made to include accurate descriptions of the important physical signs to which proper names have been applied. This, with an excellent index, makes the work valuable for reference. J. S.

A Text-book of the Practice of Medicine. By Hobart Amory Hare, M.D., B.Sc., Professor of Therapeutics in the Jefferson Medical College, Philadelphia. Second edition; pp. 1132; 131 engravings and 11 plates in colors and monochrome. Philadelphia and New York: Lea Brothers & Co., 1907.

The fact that reprintings and a second edition of this book have been so quickly called for is evidence of its popularity. The general character of the work is sufficiently well known from the previous edition. This new edition has evidently been extensively revised, in conformity with the movement of medical investigation; and in the great majority of instances the most recent work is included and referred to: for example, the status of Treponœma pallidum in relation to syphilis, the relation of the Leishman bodies to kala-azar, and many other recent investigations, are in the text, and have their proper weight given them. In questions concerning treatment, the author naturally has distinct and often very independent ideas; and in many particulars his observations regarding treatment are extremely sensible and valuable. For example, many persons still need seriously to consider carefully the importance of observations such as those made concerning the treatment of chronic nephritis, and especially the dietetic treatment of this disease; though it would have been well, from the reviewer's point of view, if, in this instance, some attention had been given to the increasing belief that high arterial tension usually has a purpose,

and, while nature may overdo this purpose, it probably is not best for the therapeutist to go so far as to keep the tension "at a point as near the normal level as possible." This however, is, still a question, to some extent, of one's point of view. The book in general is another illustration of the author's well-known capacity for collecting a vast number of facts and compressing them under one cover into an interesting systematic treatise. D. L. E.

SURGICAL DIAGNOSIS. By DANIEL N. EISENDRATH, A.B., M.D., Adjunct Professor of Surgery in the Medical Department of the University of Illinois, Chicago, Illinois. Pp. 776, with 482 illustrations. Philadelphia and London: W. B. Saunders Co., 1907.

THAT diagnosis is of vast importance no one can deny; but it is, after all, only the first step toward treatment. For as the silver hid in the mines of greedy Earth is colorless until minted and put to proper use, and as the cooking of food is futile unless it be eaten, so for a surgeon to be able merely to diagnosticate a surgical affection is for him to fall short of his highest functions. Any monograph, therefore, which deals with diagnosis alone, leaves the reader with aspirations unfulfilled, with desires unappeased, and with numerous riddles unsolved. Not only do writers on diagnosis thus lop off, as it were, their most useful hand, but those who adopt the plan of Dr. Eisendrath abstract as well the mind whose ratiocinations give the impulse by which the hand is moved. Dr. Eisendrath, by confining himself rigidly to the symptomatology of injury and disease, excludes from consideration, practically in their entirety, the subjects of etiology and pathology, without which the science of diagnosis becomes a mere art, with a dangerous tendency toward those snap diagnoses which are so brilliant when correct, and so humiliating when wrong.

Even with these disadvantages, inherent in the plan he has adopted, Dr. Eisendrath has written a notable book, and one for which the profession owes him a debt of gratitude. The illustrations form what publishers are wont to call a "feature" of the volume, and are in our opinion its most valuable portion. Indeed, we deem it a pity that the wealth of illustration is not even more profuse, and that the text has not intentionally been made to assume a subordinate role. The work would thus have become more of an atlas than a text-book, and had the author inserted the clinical histories of the patients represented, instead of attempting a systematic treatise on symptomatology, we doubt not that the usefulness of the volume would have been considerably augmented. In the limited space at his

disposal—diminished very appreciably by the elaborate system of paragraphing and display-typing which is employed—Dr. Eisendrath has been forced to treat many subjects in so compendious a manner that both the earnest student and the careless crammer will be forced to search elsewhere to satisfy himself that he has mastered the affection in question. An example is that although it is succinctly stated that injuries of the phrenic nerve cause paralysis of the corresponding half of the diaphragm, yet nowhere is there to be found a description of the symptoms present in diaphragmatic palsy. The mere fact that this is produced by lesions of the phrenic might be assumed to be familiar to a student who had acquired even a modicum of antomy, but it is far less easy to infer what symptoms will be produced. Those sections which have impressed the reviewer as least open to this criticism are those on the female breast, and on acute abdominal affections. The portions of the work treating of the injuries of the extremities are also excellent, especially praiseworthy being the illustrations showing the methods of examination in the diagnosis of fractures. Dr. Eisendrath, however, has fallen into a curious error in connection with elbow fractures: he speaks of Fig. 304, p. 472, as representing a fracture through the epiphysis, and refers to it in the text as an epiphyseal separation, whereas the illustration very clearly represents the familiar type of fracture known as the transverse diacondylar, and the structure called in the legend "upper epiphysis (capitellum) of radius" is no other than the epiphyseal centre for the capitellum of the humerus. Between this epiphyseal centre and the shaft of the humerus lies the epiphyseal line, and an epiphyseal separation occurs along this line. This error appears the less excusable, as the author frequently in the text cautions against errors in diagnosis from skiagrams, due to ignorance of the true position of the epiphyseal lines. Many of the skiagrams in the volume have been so touched up with outlines, etc., that their value as skiagrams is destroyed, while their usefulness is not as great as would be the case were they replaced by real diagrams.

It is to be hoped that in another edition, which will doubtless soon be demanded, the author will take pains to correct numerous grammatical as well as rhetorical errors in the text. The newspaper English employed is not only unscholarly, but it is ambiguous, *e. g.*, "They (fibromas) occur almost exclusively in the lower jaw, and until there is a prominence over the bone the patient is not aware of its presence." It is as a rule only extremely intelligent patients who can be expected to be aware of the presence of that which does not yet exist. The author speaks of "sequestræ," of distinguishing "a periosteal fibromata from a periosteal sarcomata," and finally informs the reader of page 535 that "if death ensues from the immediate virulence of the infection, the case may pursue a more protracted, typhoid-like course."

A. P. C. A.

A TEXT-BOOK UPON THE PATHOGENIC BACTERIA. By JOSEPH MCFARLAND, M.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College, Philadelphia. Fifth edition; pp. 647; 190 illustrations. Philadelphia and London: W. B. Saunders Co., 1906.

DR. MCFARLAND'S book upon the *Pathogenic Bacteria* has become so well and favorably known that there is little need of aught else than to chronicle the issuance of a new edition. The original plan of limiting the book to a discussion of the biological characteristics of the pathogenic bacteria has been adhered to, but much new matter has been added throughout the book, and that which had become obsolete has been eliminated. The chapters upon infection and immunity, of which our knowledge is rapidly increasing, have been entirely rewritten; they reflect very satisfactorily our present knowledge of the subjects. The book assuredly will continue to enjoy, as it merits, the favor of students and practitioners of medicine. A. K.

PROGRESSIVE MEDICINE. A QUARTERTY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia, assisted by H. R. M. LANDIS, M.D., Demonstrator of Clinical Medicine in the Jefferson Medical College, Philadelphia. Pp. 290, Vol. III, September, 1907. Philadelphia and New York: Lea Brothers & Co., 1907.

THE first article in Vol. III, for 1907, of PROGRESSIVE MEDICINE, is by William Ewart, who devotes 92 pages to an exceedingly interesting account of recent progress in diseases of the thorax and its viscera, including the heart, lungs, and bloodvessels. Among the especially important contributions are several on tuberculosis, including the report of the Royal Commission on human and bovine tuberculosis, the intestinal and glandular origin of pulmonary tuberculosis, the treatment of tuberculosis, etc.; the high diaphragm and its diagnostic significance in regard to the blood and the circulation; the diagnosis and treatment of pleural effusions; bronchoscopy as an aid to diagnosis in pulmonary diseases; the physical signs of diseases of the lungs, pleura, and heart; the diagnosis of disorders of the myocardium; disorders of the pulse; cardiac arrhythmias and heart-block; and the treatment of diseases of the heart. William S. Gottheil devotes 39 pages to recent progress in dermatology and syphilis, beginning with an important series of dermatological axioms, and continuing with a discussion of carcinoma and endothelioma of the skin, feigned eruptions, the diagnostic and prognostic

value of herpes, disorders of the nails, and syphilis in its protean manifestations. Edward P. Davis devotes 105 pages to a review of recent progress in obstetrics, comprising especially ectopic pregnancy, the toxemia of pregnancy, the complications of pregnancy, placenta prævia, septic infection, and abortion; labor, normal and abnormal; obstetrical surgery, etc. William G. Spiller devotes 40 pages to recent progress in diseases of the nervous system, especially brain tumors, aphasia, cerebral hemorrhage, tabes, paresis, multiple sclerosis, tumors of the spinal cord, epilepsy, etc. On the whole, the volume is exceedingly valuable and interesting, a worthy member of a series that should find a place on the table of every practising physician.

A. K.

A Manual of the Diagnosis and Treatment of the Diseases of the Eye. By Edward Jackson, A.M., M.D., Professor of Ophthalmology in the University of Colorado. Second edition; pp. 615; 182 illustrations and 2 colored plates. Philadelphia and London: W. B. Saunders Co., 1907.

This the second edition of Jackson's *Manual* has been brought thoroughly up to date. The student who masters it will have little that books can teach him to learn of the diagnosis and treatment of the diseases of the eye. The subject is presented with the clearness and sense of proportion to be expected from a teacher and writer like the author.

About one-sixth of the work deals with optics as applied in the study of the physiology, diagnosis, treatment, etc., of the eye—the portion which especially differentiates the study of the organ of vision from the other organs of the body. And this part of the subject is dealt with by a master. The refraction of light is made clearer, as the phenemena are referred to the waves as well as to the rays. The author truly remarks that the examination with the trial lenses requires care, system, experience, and good judgment; some excellent rules are given for the attainment of accurate results. We could wish that Dr. Jackson had been somewhat fuller in his account of the astigmatic lens—this capital device employed by him, for accurate and rapid subjective examination.

The somewhat picturesque suggestion is thrown out that homatropine or euphthalmine may be of service in some cases in making a diagnosis of incipient glaucoma (by causing an outbreak at a selected time favorable for operation). Cocaine is stated to enhance the effect of myotics in lowering intra-ocular tension. The removal of the clear lens in high myopia is still recommended in special cases, that is, when after trial it is found that the correction by glasses cannot be borne.

Judicious views characterize the work throughout. The extravagances which have been exploited in practical ophthalmology from time to time find no countenance. In short, this manual is an excellent exposition of the present state of ophthalmic science, and is to be warmly recommended to every one interested in the subject.

T. B. S.

THE PRACTITIONER'S MEDICAL DICTIONARY. By GEORGE M. GOULD, A.M., M.D., author of an *Illustrated Dictionary of Medicine, Biology, and Allied Sciences*; editor of *American Medicine*, etc. Pp. 1043; 388 illustrations. Philadelphia: P. Blakiston's Son & Co., 1907.

THE *Practitioner's Dictionary* is announced as being new in every respect and detail—not a revision of the other dictionaries that have made Dr. Gould's name well known throughout the medical world. The avowed object of the new book is to supply the practitioner with trustworthy definitions of such medical words and terms as he may need in his reading of standard medical text-books, monographs, and journalistic literature. The old and accepted features of previous lexicons have been retained; of these, the chief is a simple method, easily understood at a glance, of indicating the pronunciation and accentuation of words; and a second is the tabulation and classification of correlated terms. Of the last mentioned, however, there is one notable exception—the distribution in alphabetical order throughout the book of eponymic terms, believed to be preferable to tabulation on account of the great increase in these terms. Several valuable and important novelties have been introduced in order to make the book meet all the latest requirements: The metric system of weights and measurements in doses, etc., has been added in order to furnish the necessary equivalents to those who may prefer these to the older and more common forms; the additions and changes to the new Pharmacopœia have been inserted; and the new Basle anatomical nomenclature has been incorporated. Of the book, as a whole, one can only say that it is excellent, that it comes up to one's expectations, and fully meets all requirements. It is the most compact book of its kind—printed of large, clear type, on thin, tough, opaque paper, so that it is not more than an inch and a half thick. Its many excellent features doubtless will secure for it quite as great a measure of success as has been attained by the other dictionaries prepared by its distinguished author.

A. K.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

REGIUS PROFESSOR OF MEDICINE, OXFORD UNIVERSITY, ENGLAND,

AND

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND.

The Phagocytosis of Erythrocytes and the Question of Opsonins in Paroxysmal Hemoglobinuria.—J. EASON (*Edin. Med. Jour.*, 1907, xxi, 440) states that most of the important work under discussion at present is on the determination of the identity of the substance in the blood which exercises the opsonic function and whether this differs from the amboceptor or immune body, or is like it. Barrett gave the name hemopsonin to that substance causing phagocytosis of erythrocytes. In paroxysmal hemoglobinuria hemolysis depends on the activity of an intermediary body or amboceptor whose activity is in abeyance if the blood is maintained (in vitro) at normal temperature. Under such circumstances no hemolysis occurs, but if such blood is cooled after being mixed with potassium oxalate to prevent coagulation, and then maintained at 37° C. in an incubator for three hours hemolysis follows. Control tubes of normal blood under similar conditions show no hemolysis. Active solution of the erythrocytes by phagocytes can be seen in the pathological blood after thirty minutes in ice-water and a similar period at 37° C. This process may be partly extracellular, as by contact with the leukocytes the erythrocyte is dissolved and the hemoglobin absorbed. "Phagolysis sometimes appears to be proceeding as rapidly as hemolysis, and the erythrocytes appear to undergo very rapid solution in the medium (complement?) thus set free from the leukocytes. This process may also be observed if the inactivated serum of a case of paroxysmal hemoglobinuria is mixed with washed corpuscles and leukocytes from a normal individual and is submitted to the conditions of temperature already described. This form of phagocytosis would, therefore, not appear to be dependent on the action of a thermolabile substance or normal opsonin, but on a thermostabile substance which may be either the hemolytic amboceptor or a body corresponding to the

thermostabile opsonizing substance which may be artificially produced by immunizing an animal."

These observations may be made clinically by employing the method originally used by Ehrlich to simulate the condition of a paroxysm as follows: A ligature is put around the finger and then the finger put in ice-water (5 to 10 minutes) and then in warm water a similar length of time. Blood smears are then examined. Eason concludes as follows: "Thus it appears that phagocytosis is as much dependent on the previous chilling of the blood as is the extracellular lysis; another indication that the amboceptor is the cause of both processes."

On the Behavior of the Eosinophile Leukocytes in Cases of Pulmonary Tuberculosis.—JOHN M. SWAN and HOWARD T. KARSNER (*New York Med. Jour.*, 1907, lxxxv, 539). One of the authors (Swan) in 1904, in a study of the blood in 25 cases of pulmonary tuberculosis, came to the following conclusions: "The absence of the eosinophiles from the blood may be looked upon as an unfavorable prognostic sign. The increase of these cells while the patient is under treatment may be taken as an indication that the progress of the disease has a tendency to become arrested." This present study has to bear especially on this point and consists of the differential counts in 31 cases of pulmonary tuberculosis. In all cases 500 leukocytes were counted and the specimens were stained by Wright's method. The studies are from the Philadelphia General Hospital. In bedridden patients counts were made once a week or oftener if the case was ending fatally. In those not in bed, monthly counts were made. In a series of 31 cases, 26 were fatal and 5 were stationary or improved at the time the observations were discontinued. With the exception of 2 cases, the eosinphile cells were below 1 per cent. as a rule at periods varying from 102 days before death to the day of death. In these cases they varied from 1 to 2 per cent. for more or less lengthy periods before death. In the typically fatal cases the count was usually under 1 per cent.—as low as 0.2 per cent.; and the cells were even absent just before death. In the stationary or improved cases the eosinophilic count usually rose until discharge or discontinuance of the observations. The authors show interesting tables and charts and then append the counts of all cases in detail. They conclude as follows:

"In the light of these studies we should say that in cases of pulmonary tuberculosis the eosinophile cells tend to disappear from the circulating blood as the progress of the disease brings the fatal termination nearer, and that as the patient improves under treatment and as the disease shows a tendency to become arrested, the eosinophiles reappear in the circulating blood. It appears that this tendency of the eosinophile cells up and down may be of some use as a prognostic sign. It appears that this fluctuation of the eosinophile cells is a measure of the severity of the secondary infection with pyogenic organisms and not an indication of the extent of the tuberculous process itself; in fact the reappearance of eosinophilic cells in the circulating blood coincident with the improvement in the cases of phthisis is probably due to the removal of the chemotactic influence of the products of growth of the pus organisms and the reassertion of the influence of the tuberculin manufactured in the tuberculous lesions."

Pre-icteric Itching.—D. RIESMAN (*Amer. Med.*, 1907, ii, 79) gives a brief *resume* of the literature bearing on this interesting subject and notes that, in many reported instances, the itching preceded the jaundice by some time. He then reports in detail three cases of jaundice due to different causes, in all of which pre-icteric itching was marked. Riesman thinks that the older view that itching is due to a deposit of bile pigment in the skin can no longer be maintained. This has also been the view of several other writers. Rolleston also doubtes whether itching is due entirely to the presence of bilirubin and admits the possibility that other concomitant poisons may give rise to it or that the dry, ill nourished condition of the skin is the cause. The following facts seem to bear out the view: (1) Itching according to Frerichs and Lancereaux occurs in only about one-fifth of the cases of jaundice. (2) It bears no constant relation to the depth of the jaundice. (3) It may come and go repeatedly in a given case, while the jaundice persists undiminished. (4) The occurrence of itching that appears before the jaundice and coincidently runs with it for some time. (5) The prompt, sometimes instantaneous disappearance of the itching after drainage of the gall-bladder long before the jaundice has had time to disappear.

The cause of the itching is unknown. In all probability it is some metabolic poison or poisons which the liver in its normal state either neutralizes as it passes through in the portal blood or destroys when brought to it by the blood of the hepatic artery. The poison must be the bile, as shown by the sudden ceasing as soon as the bile is given free drainage either externally or internally. In ordinary icteric itching it most probably enters the circulation with the bile, probably by way of the lymphatics, but in pre-icteric itching or in itching depending upon hepatic disturbances without jaundice it passes into the blood independently. Riesman concludes as follows: (1) Itching sometimes precedes the onset of jaundice by a variable length of time. (2) This itching may cease the moment the jaundice is established or it may continue indefinitely. (3) Itching, whether pre-icteric or icteric, is not due to a deposit of bile pigment in the skin. (4) When itching exists for which no cause can be found, the liver, as a possible factor, should not be overlooked. (5) Pre-icteric itching is suggestive, though not pathognomonic of the existence of malignant disease involving the liver or the biliary passages. This last statement is borne out by the views of some eminent authorities, though the cases are too few for any positive opinion on this point.

The Treatment of Acute Failure of the Heart. — CHARLES BOLTON (*Lancet*, 1907, i, 870) notes that acute failure of the heart may be brought on in two distinct classes of cases: (1) The failure may be due to some organic condition affecting the heart, the blood, the bloodvessels and, therefore, initiated in a purely mechanical manner. (2) It may be the result of some nervous disturbance, such as occurs in sudden death from vagus inhibition or in cases of tachycardia. Bolton, on account of time and space, deals mainly with the first class of cases on account of its greater frequency and importance. Acute failure of the heart is brought about in two ways: By any condition interfering (1) with the emptying of its cavities during systole or (2) the filling of its cavities during diastole. As regards the first of these conditions the loss of

muscular power may be due to many acute infectious diseases or other febrile conditions, or to direct disease of the musculature of the heart, either acute or chronic. Also among the influences bearing on this first condition are the various arterial or visceral changes leading to increased resistance to the output. The second condition, interference with the diastolic filling of the heart, may be brought about by an increase or diminution in the quantity of the blood, such as may occur in various conditions.

In regard to the treatment of the acute degenerative changes Bolton lays down three indications: (1) To prevent, to stop or diminish the degenerative process; (2) to diminish the work of the degenerate heart; (3) to simulate the heart only over very short periods when fatal syncope is threatened. Bolton lays great stress on the dangers of overstimulation, goes carefully into the general treatment of the different diseases, insisting especially on the avoidance of sudden movements and overstrainings and on the cautious treatment of such symptoms as bring about vomiting, as well as the relief of excitement and shock, and other means of avoiding sudden straining efforts. The importance of absolute rest is strongly emphasized. He then passes to the treatment of the condition causing acute failure of the heart by an increase in the diastolic quantity, such as is found after undue exertion and overstraining, and the effects of altitude upon the heart, and lastly takes up the conditions causing diminution of the diastolic quantity either by vasomotor paralysis, severe hemorrhage, or increased pressure in the chest acting on the heart. This latter is seen in pericardial and pleural effusions. Shock as one of the important factors in these conditions is treated of at some length. The general treatment, management, and drugs used in the various conditions for the relief of the many different symptoms reacting badly on the heart are considered at length.

The Spleen in Organic Heart Disease.—Ernest Barie (*La presse médicale*, 1907, xix, 145) calls attention to the fact that most of the organs have received much attention and study as to their changes in heart disease, in both compensated and uncompensated cases, but the study of the spleen has been much neglected. In his list of 216 personal observations of the conditions of the spleen in organic heart disease, 79 were carefully examined after death. The remainder were examined by careful measurements and other clinical methods before death which the author enumerates at length. In about two-thirds of the cases the spleen was of normal size, but in about one-third there were more or less changes, hypertrophy, diminution in size, the presence of infarcts. In the 20 cases of hypertrophy of the spleen the liver was usually enlarged in like extent. The spleen in 2 cases weighed 630 and 860 grams. The others weighed less and showed marked chronic passive congestion. In 4 cases the volume of the spleen was diminished, a marked atrophic condition being evident. Infarcts were found in 13 of the 79 autopsies. As a rule, in all the cases of abnormal spleen there were more or less serious diseases in the past history of the patient, and it is possible that they may have had some influence on the subsequent condition during a cardiac breakdown.

As regards the clinical signs and symptoms, those associated with the atrophic spleens are somewhat vague, while the diagnosis of infarcts

was difficult; sudden local pain and slight enlargement of the spleen helped in their detection. In the cases of enlarged spleen a real "splenohepatic asystole" was induced and is characterized, contrary to the usual form, by a regularity of the pulse, absence of venous stasis, cyanosis, or oliguria, while, instead of the classical red and hard œdema, the œdema is white and soft. There was also pallor and frequent epistaxis, the latter sometimes being so severe as to require tamponing. Barié says: "Besides the pallor and the severe epistaxis, the progressive debility is the third chief important symptom in this 'splenohepatic asystole.'"

SURGERY.

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSISTANT SURGEON TO THE UNIVERSITY AND THE PHILADELPHIA GENERAL HOSPITALS, AND INSTRUCTOR IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA.

Internal Intestinal Fistulæ.—HOFMEISTER (*Beit. zur klin. Chir.*, 1907, liv, 745) says that abnormal communications between two small intestines or between a small and a large intestine are rare, aside from those produced by operative anastomoses. They have been found, chiefly, postmortem. In life they have been recognized in rare cases, as when a relatively free communication existed between an upper and a lower intestine. This might give symptoms that would render a diagnosis possible. Usually, however, the symptoms produced are not sufficiently definite to aid in the diagnosis. Among the causes of these internal fistulæ, according to Hilgreiner, are: tuberculous peritonitis, abscesses around a foreign body, actinomycotic abscesses, the breaking through of the closed end of a Meckel diverticulum. In the fistulæ between the small and large intestines carcinoma plays an important part. The peptic jejunal ulcer following gastro-enterostomy is of interest especially with regard to the possibilities of diagnosis and treatment. Hofmeister reports a typical case that has not hitherto been reported, in which the intestinal fistula had a traumatic origin. A boy, aged six years, suffered from many attacks of severe, paroxysmal, abdominal pain, difficult defecation, and frequent passages of blood in the form of lumps or masses. He became so emaciated, apparently from a deep-stated ulcerating stenosis of the intestine resistant to internal treatment, that one had to choose between leaving him to his fate or risking a fatal termination by operation, with the object of putting out of function the diseased portion of the intestine. This was done, but it did not help materially in the diagnosis, *i. e.*, of establishing the presence of a communication between the portion above and that below the artificial anus.

The mother had said that from time to time, since the artificial anus had been present, a movement by the rectum had occurred, but this fact had been overlooked. A second operation was done and a mass of adherent intestine was resected. This showed a fistula in that portion of the intestine leading to the artificial anus. An ileocolostomy was then performed, which was followed by undisturbed healing. The kick which the patient had received in the abdomen had evidently produced a wound of the intestine which led to a localized peritonitis with abscess formation between the neighboring intestines and perforation of the abscess on three sides. Healing of the abscess followed, but there was persistence of the fistula opening into three portions of the intestine.

The Technique of Pancreatectomy.—DESJARDINS (*Revue de chir.*, 1907, xxvii, 945) says that the pancreas for surgeons is a noli tangere, since they do not dare to remove it as they do other organs. It should not be regarded as so inaccessible as formerly, with the advantage of Mayo-Robson's cushion and his or Kehr's incision. The control of hemorrhage is better understood, so that the fear of the important bloodvessels associated with this organ should not be so great. Desjardins says that the removal of the pancreas is not incompatible with life, and that the biliary passages can be reëstablished without undue loss of time. Billroth, in 1894, and Franke, in 1901, have done the only 2 total pancreatectomies, both with success. Neither patient, afterward, presented any troubles due to loss of the organ.

Many partial pancreatectomies have been performed. Of 30 collected cases, there were 9 partial resections of the tail, all but 3 for malignant tumors. There were 2 complete resections of the head, and these alone, Desjardins calls true partial pancreatectomies. There was one in which the body of the pancreas was removed, leaving the head, which avoided sectioning the common bile-duct, and left the tail. This was done for a chronic sclerotic pancreatitis.

Of the 30 cases, there were 16 operative cures and 14 deaths. Of the 2 total pancreatectomies, both were cured; of the resection of the tail, 7 cures and 3 deaths; of the partial of the head, 7 cures and 9 deaths; of the total of the head, 2 deaths. In spite of the good results in Billroth's and Franke's cases, Desjardins does not think that we have a right to do total pancreatectomies, the partial alone being justified by physiology. It is necessary to remove the corresponding part of the duodenum with the head of the pancreas, since both are supplied by the same bloodvessels, they are intimately adherent to each other, and since it is necessary to remove also the retroduodenal lymph glands. The three dangerous zones are: first, where the ascending colon is adherent to the second part of the duodenum. It is necessary here to avoid wounding the colon. The second zone is where the mesenteric arteries emerge from the border of the pancreas, passing in front of the duodenum. The middle colic artery may here be wounded, giving rise to gangrene of the transverse colon. The third danger zone is posterior, where the portal vein and inferior cava are in danger. All three zones can with care be avoided. The careful detachment of the parts is the key to the success of the operation. The head of the pancreas and the duodenum surrounding it are detached en bloc, the

duodenum near the pylorus and the beginning of the jejunum being divided between clamps. The common bile duct is divided as near as possible to the duodenum, and the body of the pancreas, including the duct of Wirsung, is divided also. When the removal of the head of the pancreas and the duodenum has been concluded, the pyloric end of the stomach is closed, and the upper cut end of the jejunum is implanted into the stomach, making a gastro-enterostomy. The open ends of the common bile duct and the freed end of the duct of Wirsung are implanted into the upper end of the jejunum, one on one side and the other on the other side. The cut surface of the pancreas is tied off in sections around its duct for hemostasis.

This operation is possible only when the common bile duct and the duct of Wirsung are dilated sufficiently to receive the button of Boari, which is employed to make the connections with the jejunum. In such a case about 30 cm. of the upper end of the jejunum is cut off from the rest, still preserving its attachment to the mesentery. The then upper end of the jejunum is employed for a gastro-enterostomy. The isolated piece of jejunum is anastomosed by one end to the gall-bladder and by the other end to the cut end of the pancreas, hemostasis having been previously effected in this stump. The bile and pancreatic fluid can thus escape only through this new common passage-way made up of the isolated portion of jejunum, which is now anastomosed to the remaining jejunum just below its attachment to the stomach.

The Mesocolic Route: Cholecystojejunostomy, Transmesocolic Gastro-enterostomy.—LOTHEISSEN (*Zentralbl. f. Chir.*, 1907, xxxiv, 605) says that the posterior retrocolic gastro-enterostomy is considered by most surgeons as the normal method. The only objection to it is the occasional occurrence of a vicious circle. Lotheissen has yet to see a failure with it in either v. Hacker's clinic or his own. Brentano has recently shown that the anastomosis between the gall-bladder and the jejunum should be done through the mesocolon. Lotheissen recommended this operation in 1903. The suture is easily carried out after the opening in the gall-bladder has been made. The intestine is tied off with a strip of gauze as in a gastro-enterostomy, and the gall-bladder, after the abdomen is packed off with gauze, is carefully punctured and completely emptied. This permits one to palpate the head of the pancreas and to exclude stones in the common duct. When the operation is completed the gall-bladder lies in the opening of the mesocolon and the visceral situation is normal. The peristaltic movement is unchanged. In doing a gastro-enterostomy, Lotheissen also works through an opening in the mesocolon, in this way doing a posterior gastro-enterostomy. Only once was it necessary to anastomose the jejunum to the anterior wall of the stomach. It is often impossible to bring the transverse colon upward to expose freely the posterior stomach wall. After the operation is completed through the mesocolon, this is closed with a few sutures.

Suppuration of the Hand and Forearm.—KANAVEL (*Zentralbl. f. Chir.*, 1907, xxxiv, 1001) reports the results of experimental and clinical studies on the seat and paths of extension of suppuration in the hand and forearm. The influence of the tendon sheaths was not taken into

account. A series of sections was made of the hand and forearm and the connective tissue picked out. Injections were employed to determine the manner and paths of extension along the connective-tissue spaces under varying pressures. Pertinent clinical observations together with the experiments led to the following conclusions:

Extension of the pus from the fingers occurred through the canal for the lumbricalis muscle, to the cavity of the hand and back along the lumbricales, avoiding the tendon sheaths. This was observed clinically and experimentally. Pressure on the hand forced pus in the central connective-tissue space of the hand to the level of the metacarpophalangeal joints, through the lumbrical canals. Extension between the metacarpal bones seldom occurred. Pus passing under the anterior annular ligament to the forearm will be found almost always under the deep flexors of the fingers. In the middle of the arm the pus will almost always be found to be more superficial, lying between the muscles in the neighborhood of the median and ulnar nerve as well as the ulnar artery. It then extends distalward along the course of the ulnar artery, which accounts for the occasional occurrence of secondary hemorrhage.

Palmar abscesses should be evacuated in the course of the lumbrical canals, every infected canal being opened. When the pus originates in the fingers it can be found in the layer over the tendon sheaths of the palm. In protracted cases a large collection will be found in the space under the tendons. In the first group of cases, a simple incision will be sufficient; in the second group a closed forceps may be pushed between the tendons at the upper end of a communicating canal and then the blades opened. If the tendons are not necrotic or the tendon sheaths involved, this procedure will be followed by quick healing. If the thenar space alone is involved, the same method may be employed, passing the forceps from the radial side of the hand. If the central space of the hand is also involved, the forceps should be pushed laterally across and through to the ulnar side. A rubber drainage tube may be left in for a few hours. Rapid healing, with complete cure and return of function, usually results. If the forearm has been invaded the palmar incision may be extended upward through the anterior annular ligament. In a greater number of cases a better result was obtained by lateral incisions in front of the ulna and radius about 3 or 4 cm. above the wrist-joint. The forceps is then pushed across the forearm on the flexor side. The nerves and bloodvessels will be avoided if the forceps is kept close to the bones.

Concerning Ligature of the Common Carotid. A New Method of Ascertaining the Possible Disturbances of the Circulation.—JORDAN (*Arch. f. Chir.*, 1907, lxxxiii, 23) says that in 25 per cent. of the cases reported by Pilz, Zimmermann, and Krankepuhl, brain disturbances occurred and 10 per cent. died. Since we cannot ascertain how abundant are the collateral vessels, nor their capacity for dilatation, it is always difficult to determine the prognosis of a ligature of this vessel. To overcome this difficulty Jordan recommends a method which he has tried, successfully, on animals and in one case on man, *i. e.*, the previous, temporary, not firm ligature of the carotid for forty-eight hours. Since the brain symptoms dependent upon a lack of nourishment to the brain occur immediately after the operation, at the end of the first or in the

course of the second twenty-four hours; if no trouble from the ligature occurs during this time it is unlikely that there will be any grave consequence from occlusion of the carotid. Experiments on lower animals showed that the ligature did no damage to the intima. Senger, in 1895, employed the temporary ligature for the bloodless extirpation of a tumor of the thigh. The operation should be done under local anesthesia, in order that the effect on the brain may be observed, and the ligature withdrawn on the first appearance of any distinct symptoms. The ligature material may be a small linen band, a rubber band, catgut, or a forceps with its blades guarded with rubber covering. The chief point is to apply the constriction very carefully, until the temporal pulse disappears. A further indication for this procedure is to be found in the suture of arteries.

The Technique of Direct Transfusion of Blood.—CRILE (*Annals of Surgery*, 1907, xlvi, 329) bases his remarks on 225 experiments upon animals and 32 clinical cases. The blood was transferred from the artery of the donor to the vein of the recipient. In the clinical transfusions the radial artery of the donor and the proximal end of any superficial vein of the arm of the recipient were employed. Unless contra-indicated, both patients are given a hypodermic injection of morphine twenty minutes before the transfusion begins. The donor is placed on a Trendelenburg table, so that if he should become faint the head may be readily lowered. The recipient is placed upon an operating table with his head in the opposite direction. Infiltration anesthesia of 0.1 per cent. cocaine solution is employed, and the radial artery is exposed. A Crile clamp is applied to the proximal end of the artery and the distal end is ligated; the artery is divided; the adventitia pulled over the free end as far as possible and closely snipped off; a moist sponge now covers this field; 3 or 4 cm. of a superficial vein of the recipient is then likewise freed; the distal part ligated, the proximal closed with a Crile clamp; the distal part is divided with scissors, the adventitia drawn out as far as possible and closely snipped off; the vessels are then inspected and a cannula whose bore is larger than the actual tissue thickness of either vein or artery is selected. The vein may then be pushed through this tube, after which the freed end is turned back like a cuff and snugly tied in the second groove. The artery is then drawn over the vein and tied in the first groove with a small linen ligature. This completes the anastomosis. The clamp is then removed from the vein; afterward, gradually, from the artery; when the blood stream will be seen to pass from the artery across to the vein, dilating the latter. By this method intima comes in contact with intima, the blood is transferred without clotting. The blood lost by the donor is regained in from four to five days, and the amount transferred is under the immediate control of the operator. The rate of transference should be carefully gauged, because of the risk of overcharging the pulmonary circulation.

Ligation of the Ductus Arteriosus.—MUNRO (*Annals of Surgery*, 1907, xlvi, 335) reports a case of a healthy girl baby, that soon after birth exhibited symptoms of some cardiac lesion, out of keeping with the general appearance of perfect health and development. On severe

exertion, such as straining at stool, it would become cyanotic and the cardiac beat would cease. At times the child would apparently die, only to recover as soon as the heart was stimulated with electricity. In a few weeks atelectasis developed, for which artificial expansion of the lungs under negative pressure in a pneumatic cabinet was tried. This met with only temporary success. Auscultation at this time revealed a cardiac murmur with the pulmonary rales, but cyanosis was not a marked feature. After death, which took place without œdema or marked cyanosis, examination showed an open distinct ductus arteriosus, lying easily within reach behind the sternum, without any other defect except a dilated right ventricle. Munro made further dissections and satisfied himself that it would be possible to ligate the duct, provided the diagnosis could be made beforehand. In the newborn the duct of Botalli is a little over 5 mm. in diameter and 10 to 15 mm. long. The length increases generally up to the time of obliteration, which, normally, is complete by the twentieth day. This period of patency is, therefore, normal. Townsend examined 100 newborn babies during the first three days of life, to throw some light on a pathological patency, but he was unable to hear anything instructive. In typical cases the foramen ovale is closed.

Concerning the operation which may be practised on these cases, Munro says that the sternum may be split along its centre with a knife. Retraction of the sternal halves, gives ample room. The right pleural cavity will, probably, be opened, but the left one will not. After retracting the thymus upward, the pericardium is exposed. Its reflection lies so high on the large vessels that the ductus, to all intents and purposes, is intrapericardial. In the upper angle the aorta will be seen on the patient's right and the pulmonary artery on the left. By following close to the aorta toward the under surface of the arch, the ductus, as large as the aorta itself, will be seen as the first vessel to the left, pointing upward and a little to the right. On pushing through the tissues by blunt dissection, the ductus, theoretically, should be easily surrounded by a ligature. Simple crushing might accomplish as much and is worth trying. After closing the anterior pericardial wound the sternum can be sutured or not and the skin closed.

Technique of Bloodvessel Suture.—SWEET (*Annals of Surgery*, 1907, xlvi, 350) believes that the exact end-to-end approximation is easier of execution than other methods; and since it accomplishes that great desideratum, the restoration of tissues as nearly as possible to their original position, it is perhaps theoretically correct. There is a unity of opinions that the suture material should be of fine silk, of a size carefully chosen so that it will completely fill the hole left by the needle, which should be of the smallest possible size, round, either straight or curved, according to the preference of the operator and the site of operation. Experimenters are further agreed that the stitches should include all the coats of the vessel, since the penetration of the intima is a matter of no consequence. All insult to the vessel wall, such as grasping it with forceps, must be rigidly avoided. If the edges of the wound have been crushed they should be refreshened by resecting a bit with a sharp scalpel; since the cut of a scissors is always a crushing one, they should not be used. Three tension sutures of fine silk, impregnated with vaselin, are

then laid at equidistant points of the circumference of the vessel ends. An assistant then applies traction to two of these guide sutures in turn, stretching the portion between two sutures into a straight line, facilitating the laying of the continuous suture, and preventing a narrowing of the lumen. If the third tension suture is weighted with a hemostat, the vessel will be arranged in the form of a triangle, and there will be no danger of catching the opposite wall while laying the suture, which is a continuous overhand stitch. The separate stitches should be drawn just tight enough to secure absolute approximation, but not too tight, else the tissues be everted; they must be laid very close together. Absolute asepsis is necessary. Sweet concludes that in any case in which the anastomosis of a bloodvessel is indicated it should be tried; aneurysms and secondary hemorrhages should not occur. If immediate thrombosis occurs, we should be as well off as though the vessel had been ligated; if gradual thrombosis occurs we might well hope that such a process would be more favorable to the formation of a collateral circulation than would immediate ligation.

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD WEBB WILCOX, M.D., LL.D.,

PROFESSOR OF MEDICINE AND THERAPEUTICS IN THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL; VISITING PHYSICIAN TO ST. MARK'S HOSPITAL,

ASSISTED BY

HENRY HUBBARD PELTON, A.M., M.D.,

INSTRUCTOR IN MEDICINE IN THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL; CHIEF OF THE MEDICAL CLINIC, PRESBYTERIAN HOSPITAL DISPENSARY, NEW YORK.

Drugs in Diabetes.—WILLIAMSON (*The Practitioner*, lxxix, 1, 136) states that in large doses opium, morphine, and codeine sometimes diminish the sugar excretion in diabetes, more especially in the mild types of the affection; their great disadvantage is their tendency to cause constipation, and as this increases the liability of the patient to coma, these drugs do not appear to be suitable in the aggravated types of diabetes. Heroin also has been tried, but this also, while its use may be beneficial in the less severe forms of the disease, may tend to constipation and occasionally produces toxic symptoms. Sodium salicylate and aspirin are often more satisfactory than opium or its alkaloids, and in mild types of diabetes may induce a diminished sugar excretion, but in the severe forms this benefit seldom occurs, although the general condition of the patient may be improved. The doses should be such as to avoid inducing toxic symptoms, and aspirin is often preferable to the sodium salt on account of its less liability to be followed by ill-effects. Bismuth salicylate is often very useful in instances complicated by diarrhœa, but in the absence of this manifestation it cannot be

continued for any considerable period. After giving up treatment by these drugs the amount of sugar in the urine is only too prone to increase again. Nevertheless a certain benefit is to be attained by the administration of these agents. In the presence of diacetic acid in the urine and the imminence of coma the alkalies, particularly sodium bicarbonate, in connection with free purgation by means of mercurials, may cause a disappearance of this dangerous manifestation, but at times this form of treatment is without avail in this regard, especially if the diacetic acid reaction is marked, although the alkaline treatment may be of temporary service in improving the general condition and delaying the onset of coma. The amount of the salt given may be as much as an ounce or more in twenty-four hours, and when premonitory symptoms of coma are present an ounce and a half may be given for several days in succession. When coma has commenced the symptoms may sometimes subside under the influence of large doses of the bicarbonate, but this manifestation is very likely to recur at a later date.

Tuberculin Treatment.—JEANS and SELLARDS (*Johns Hopkins Hosp. Bull.*, 1907, xviii, 195) have studied nine patients treated by means of tuberculin of their own preparation, the treatment having been carried out in accordance with observations of the tuberculo-opsonic indices of the patients in hand. They consider that the study of these nine patients is sufficient to justify the continuation of the method of treatment. In none of the patients has the result been miraculous, but in two, at least, there seemed to be a very definite relationship between the treatment and the improvement of the patient. It is held as important that, in addition to the tuberculin treatment, hygienic measures should be carried out as well. The patients are too few for any general conclusions to be drawn. Other dosage and other interspacing of dosage might have been more effective and perhaps other forms of tuberculin might give still better results. This can be decided only by the clinical results and not, in the author's opinion, by the opsonic curves.

Atoxyl in Syphilis.—UHLENRUH, HOFFMANN, and ROSCHER (*Deut. med. Woch.*, 1907, 22, 873) have found that injections of atoxyl markedly influence the infection in animals inoculated with syphilis. Their first trials in human beings failed because of too small dosage, but the results of later attempts with larger doses were more successful. One patient in whom the small doses were ineffectual was quickly cured when the amount administered was increased to 7½ minims. In another, syphilis of nine months' duration which had proved refractory to ordinary treatment, nine injections caused a rapid amelioration of the numerous syphilitic ulcers. In a third patient dressings of 10 per cent. atoxyl were followed by a rapid healing of the ulcerations; those which were treated locally healed more quickly than others not dressed, even though injections of the agent were employed at the same time. The injections should be given into the muscles of the thigh; they are painless and cause no local reaction, although they may be followed by anorexia, insomnia, colicky pains and, rarely, by albuminuria. Atoxyl appears to be a true antisyphilitic, especially active early in the disease and in the ulcerations of the early stages.

Transfusion of Blood in Severe Anemia.—MORAWITZ (*Münch. med. Woch.*, 1907, xvi, 767) has employed transfusion of defibrinated blood, about six ounces having been injected at each dose, in six patients. Two of these have been observed too short a time for definite conclusions to be drawn other than that a subjective improvement has taken place. In another patient the treatment was a failure, but in the other three the results were striking. One of these had grown progressively worse under the administration of arsenic, but under the injections of defibrinated blood the blood soon became normal. The other two patients, in whom the prognosis had been unfavorable, improved markedly under the injection treatment. Objective and subjective results show themselves in three or four days after beginning treatment. No serious by-effects were noted.

Thiosinamine in Cardiovascular Fibroses.—RENON (*Revue thérapeutique*, 1907, xiii, 443) has employed injections of thiosinamine on account of its properties in softening cicatricial tissue in instances of cardiovascular fibrosis, valvular affections, and arteriosclerosis. He injects from 15 to 30 minims of a 4 per cent. solution under the skin of the abdomen every two days. The injections are well-borne, only slightly painful, and cause no inflammatory reaction. In mitral lesions the results were *nil*, but in aortic affections a noticeable effect was observed, the dyspnœa being lessened and the arterial tension lowered. The physical signs remained unchanged. In arteriosclerosis the effect was less constant, but in certain patients the dyspnœa became less and the blood pressure was lowered. The action of the drug lasted from three to four months.

The Intravenous Dosage of Digalen.—KOTTMANN (*Correspondenz-blatt f. Schweizer Aerzte*, 1907, x, 306) states that this drug is frequently employed in the medical clinic of Berne in patients affected with cardiac insufficiency. Experience has shown the intravenous dosage to be as follows: 15 minims is sufficient to obtain a therapeutic effect, although the usual minimum amount given is five times this quantity. In case the small dose is not followed by definite results the injection may be repeated in a half-hour. The injection is usually followed by a feeling of improvement and an amelioration of the symptoms. Sahli considers that this fact is important from a standpoint of the study of the action of the heart muscle, and is an index as to whether or not digitalis is indicated in a given patient. The injections should be given slowly into the muscular tissue, and it is advisable to induce venous stasis of the part by means of an elastic ligature applied above the site of the injection.

The Three Doses of Digitalin.—HUCHARD (*La quinz. thérap.*, viii, 8, 177) writes of the three methods of prescribing digitalin thus: (1) *The massive dose.* This is given when an anti-asystolic and diuretic action is desired. The amount prescribed is 50 minims of a 1 to 1000 solution, to be given once or twice in a single day. In from thirty-six to forty-eight hours an abundant diuresis is established, with increase in the strength of the cardiac action, relief of the visceral congestion and œdema, and increase in the elimination of the chlorides. If the effect is insufficient the dosage may be repeated in eight or ten days. (2)

The small dose. This is the sedative dose and is given to relieve palpitation and dyspnœa, such as occur in mitral stenosis during the period of compensation. It consists of 5 to 10 drops of the 1 to 1000 solution daily for about five days, every three or four weeks. This quantity of the drug prolongs the diastole. Mitral stenosis is perhaps the only cardiac lesion in which digitalis is indicated during the period of compensation. (3) *The very small dose.* This is the cardiotonic dose; it has no diuretic or true cardiac action, and may be continued for weeks or months with intermissions at intervals of from fourteen to twenty-one days. The proper amount is 3 to 4 minims of the 1 to 1000 solution; this dosage is unlikely to cause more than very mild toxic symptoms, and these occur only because of the slowness of the elimination of the drug. The digitalin solution is given hypodermatically, or tablets of equivalent strength may be substituted if it is desired to employ oral administration.

Veronal as a Hypnotic.—FOXWELL (*Folia Therap.*, 1907, i, 69) in a comparative study of drugs of this class voices the statement that veronal is, taken altogether, our most satisfactory hypnotic. Its action is sure, powerful, and not accompanied by untoward by-effects. Rarely giddiness, headache, vomiting, and transient eruptions have been noted, but no serious complications. As a simple hypnotic 3 grains is a sufficient initial dose; seldom, except in mental patients, will more than 7 or 8 grains be required. Cumulative action is likely to occur, but there is probably no danger of any sudden *dénouement*, though there may be an increasing effect from continuance of its administration in the same dosage. The drug is an excellent sedative in doses of 1½ to 2 grains thrice daily. As a hypnotic, given in hot water, milk, or tea, it usually induces sleep in a half-hour. The slumber is quiet and natural and, if the dose has been small, no unpleasant heaviness is experienced on awakening.

Aspirin and Sodium Salicylate in Rheumatic Conditions.—ROCH, JEANNERET, and LAMUNIERE (*Therap. Monats.*, 1907, xxi, 239), after a comparative study of these two drugs, draw the following conclusions: To those who know how sensitively rheumatic patients react to sudden diminution of the dosage of sodium salicylate, it seems strange that one can without untoward effect change suddenly from doses of 75, 90, or 100 grains of sodium salicylate to 45 grains of aspirin. The latter has fewer unpleasant effects upon the alimentary tract than the sodium salt, and is superior to it in the treatment of obstinate subacute rheumatism, even when exacerbations are likely to take place. The action of aspirin is explainable on the theory that while it is transformed in the intestine and its elimination product is identical with that of sodium salicylate, it is absorbed more slowly and with greater regularity than is the latter substance, and the organism consequently becomes more saturated with the salicylic acid. Over and under saturation are much more easily controlled in treatment with aspirin than in treatment with sodium salicylate. It seems probable that the nervous symptoms, headache, tinnitus, delirium, etc., which are not uncommon results of the administration of the salicylates, may be avoided when aspirin is employed, for the reason that the absorption of this drug is so continuous and regular.

The Standardization of Cardiac Remedies.—EDMUNDS (*Jour. Amer. Med. Assoc.*, 1907, xlviii, 1744) draws certain conclusions upon this subject, among which are the following: The necessity for a uniform strength of the cardiac tonics upon the market is undeniable, but how this is to be obtained is another matter. If the tinctures are standardized those of an individual firm may be uniform, although this does not necessarily follow; but each firm having its own standard, there can be little more uniformity than at present. What is needed is a national standard such as the Pharmacopœia furnishes for chemical assays. As the matter now stands the physiological assay is made by the physician at the bedside. He gives the drug for a reasonable time and gets no effect perhaps, and then has to increase the dose until the desired action is attained. No amount of standardization would ever do away with his ascertaining the physiological dose for the individual patient, but it certainly would shorten the process and avoid the loss of much valuable time, which may mean the life or death of the patient. [If the mandates of the Pharmacopœia are obeyed any manufacturer can produce uniform and official preparations.—R. W. W.]

PEDIATRICS.

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.,

OF PHILADELPHIA.

The Treatment of Some Common Tuberculous Affections in Children.—C. R. KEYSER (*British Journal of Children's Diseases*, 1907, iv, 277–281) finds "subcutaneous tuberculous foci" quite commonly in children. They form small, round masses in the subcutaneous tissues, and are freely movable under the skin and the deeper structures; occasionally they occur in the deep cellular tissue. Later the skin becomes reddened, tender, and still later growth and skin adhere and the tuberculous mass breaks down. They are most common on the limbs, but have nothing to do with disease of the bone; they are precisely similar to gummas forming in the same situation. The treatment should not consist of incision and drainage, as the "abscess" does not contain a drop of true pus. Very often, if this is done, pyogenic organisms are admitted into the cavity and true pus forms.

The treatment he advises is incision and complete evacuation of all the contents, most particular attention being taken to remove all the semisolid caseous masses, and to scrape away the so-called pyogenic membrane. The scrapings, etc., should be removed with normal salt irrigation, the cavity filled with iodoform emulsion and the wound accurately sutured and pressure applied. Re-accumulation should be treated by aspiration and pressure. He treats tuberculous osteomyelitis by laying the bone freely open, scraping away all the tuberculous matter, filling the cavity with decalcified bone chips, suturing the wound, and applying a splint.

A Case of Morbus Cordis.—T. R. WIPHAM (*British Journal of Children's Diseases*, 1907, iv, 252) reports a case of heart disease, in which there had been 7,800,000 red blood corpuscles per c.mm. The patient was a girl, aged eleven years, who was subject to frequent attacks of epistaxis. The heart was much enlarged, and there was a thrill at the apex and at the base, especially over the aortic area. Presystolic and systolic murmurs were present at the apex, and the latter was loud and rough at the base, especially to the right of the sternum. The second sound occasionally could be heard in the pulmonary region, but only faintly; elsewhere, it was entirely absent. There was no cyanosis or clubbing of the fingers. The patient had recently had acute rheumatism, but there was no history of a previous attack or of chorea. The diagnosis suggested was mitral stenosis and possibly a congenital narrowing or coarctation of the aorta.

Tuberculous Disease of the Spine in Children.—OLIVE ELGOOD (*British Journal of Children's Diseases*, 1907, iv, 229–252) considers spinal caries an inaccurate name to give to all forms of tuberculous disease of the vertebræ. A primary, superficial caries does occur fairly frequently in adult life, but in children this type is rare. The disease conforms primarily to one of two pathological types: (*a*) The localized soft, caseous deposit, or the sequestrum, in the interior of the bone, which is the usual form met with in children; (*b*) the primary superficial caries. In the former tubercle bacilli become deposited from the blood in the cancelli of the vertebræ, and give rise to a collection of epithelioid cells, which either become differentiated into round areas forming microscopic or macroscopic tubercles, or remain undifferentiated as diffuse, infiltrating tuberculous tissue. In either case an area of simple inflammatory round cells occurs round the specific formation due to the irritation set up, primarily by the pressure of the latter in the surrounding normal tissue, and secondarily to the gross weight of the trunk above the seat of the disease pressing on the softened vertebræ. As the tuberculous disease spreads into and replaces the granulation tissue, the latter extends into the normal bone, progressively absorbing it, while in the central part the tuberculous tissue either breaks down into caseous pus forming the soft tuberculous deposit, or may, in parts, caseate and in other parts organize into fibrous tissue and sclerosed bone, which then comes to lie in caseous pus, forming sequestra; the latter are not frequently seen in children. The disease ultimately reaches the surface, either at the front or sides of the body, or it perforates backward into the spinal canal. After reaching the surface of the body it may continue as a secondary superficial caries, spreading along the surface of the bodies and destroying the intervertebral disks, or it may form a localized abscess, surrounding the spot where the caseous pus has reached the surface.

Primary superficial caries is due either to a primary deposit of tubercle in the periosteum or surface of the bone, or is the secondary result of the perforation of an internal deposit on to the surface. The disease being on the surface spreads rapidly to the adjacent soft parts, giving rise to the typical tuberculous abscesses of the various regions. In rare cases the disease occurs in the transverse processes, or spines, and then quickly gives rise to an abscess, the disease being so near the surface.

Spinal caries is not so common as hip disease in children, the former making up 27 per cent., the latter 39 per cent. of the cases seen by Elgood. Traumatism preceding the caries was found in but 14 per cent. of Elgood's cases. Girls made up 33 per cent. of her cases, and the resisting power of their blood to bacterial invasion of bones was invariably greater than in boys. A family history of tuberculosis was present in 6 of her cases. From the standpoint of clinical signs the author makes the following classification: (1) Early cases before the establishment of curvature, only diagnosticated by the determination of the presence of rigidity of the spine. (2) Cases with the establishment of spinal deformity, but without complication. (3) Cases with or without deformity, but with complication: (*a*) abscess; (*b*) some concomitant tuberculous trouble, such as tuberculosis of the lungs or glands, joint and bone affections; (*c*) sepsis; (*d*) compression of the spinal cord.

The treatment is classified under the following headings: (*a*) *Conservative methods:* This means rest and is suitable in the very early and uncomplicated cases. Supine position in bed with extension to each leg and counterextension to the head in cervical disease cause the pain to cease within twenty-four hours; the patients are kept thus for six weeks after the last complaint of pain. This is followed by a plaster-of-Paris jacket, and in upper-spine cases a jury-mast is incorporated in the layers. The patient is kept on his back for one year after application of this support, and permitted to move sparingly the next year. Weakness of the back, thereafter, is best met with slight kneading massage of the muscles of the back, combined with a light support. (*b*) *Operative procedures:* The removal of pus under the strictest aseptic precautions; this is not curative. Laminectomy for the purpose of removing the whole area of the disease; 1 patient thus treated died of meningitis, 2 others recovered. Laminectomy for the purpose of reducing deformity; this should only be performed in the late stages of quiescence of the disease, and should be very carefully considered, before being undertaken, as it may easily light the process up again. (*c*) *Vaccine treatment:* This can only be an adjunct to one of the former methods described. Injections of tuberculin can be combined advantageously with any of the methods.

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Advanced Ectopic Gestation.—SITTNER (*Archiv f. Gyn.*, 1907, Band lxxiv, Heft 3) reports 2 cases of abdominal pregnancy. One was that of a woman pregnant for the fourth time, having an indefinite swelling to the right of the uterus. Appendicitis was suspected, and

pain and collapse occurring, led to a diagnosis of ruptured ectopic gestation. The patient was not subjected to operation, and the uterus continued gradually to enlarge. At about the seventh month abdominal section was performed, and abdominal pregnancy was found, the placenta being attached to the intestine over the right pelvic region. Sittner calls attention to the difficulty of diagnosis in cases of abdominal pregnancy, which is frequently not made before operation. In 77 cases of ectopic gestation in Schauta's clinic, the diagnosis of an inflammatory condition in the Fallopian tube was made in 7. When the uterus ruptures in early pregnancy the diagnosis is especially difficult.

When the child is living, operation gives a high mortality, which is gradually lessened after the child dies. The mortality of ectopic gestation without operation is stated as 68 per cent., and 23 per cent. in those operated upon. The death of the fœtus does not entirely do away with danger from placental hemorrhage, as the placental vessels are not completely obliterated for six months after the death of the fœtus. If the diagnosis can be made, it seems probable that early operation while the child lives is least dangerous for the mother. The mortality among children born after ectopic gestation is, during the first twenty-four hours, nineteen times greater than in cases of entopic pregnancy. These children are ill-developed, and but about 50 per cent. of them reach adult life. Delay in operation is dangerous for the mother, from peritonitis, diseases of the bladder, emaciation, and rupture of the sac. While the complete removal of the placenta has been considered exceedingly dangerous, in 107 cases of ectopic gestation the placenta and membranes were removed in 53; in 54 cases the placenta was left; when it was removed, the mortality was 18.8 per cent.; while in cases in which the placenta was allowed to remain the mortality rose to 57.4 per cent.

Among the difficulties experienced in removing the placenta, in 10 per cent. extensive adhesions were present; the placenta was situated within the folds of the broad ligament in 25 per cent., and attached in an atypical position in the pelvis in 37 per cent.

Sittner's paper is based upon 126 cases in which section was done after the tweny-first week of pregnancy, with a living child. The literature on the subject shows 14 cases in which one operator has twice operated for abdominal pregnancy at full term with a living child. In only 4 instances has the same operator had 3 such cases. Sittner believes that most cases of secondary abdominal pregnancy develop through actual rupture of the muscular tissue of the Fallopian tube, occurring after erosion. This develops gradually, and tends to explain those cases of abdominal pregnancy without symptoms of tubal rupture. When rupture is sudden as the result of violence, the sac of the ovum is loosened and pregnancy ceases to progress.

The Lymphatic Glands in Pregnancy.—MEYER (*Surg., Gyn., and Obstet.*, May, 1907) has studied 59 cases in the obstetric wards of the Johns Hopkins Hospital to determine the condition of the lymphatic glands. These patients were palpated weekly from two to twelve weeks. The greater number of examinations were made before labor. The age of the patients varied from sixteen to forty years. About

25 per cent. were between sixteen and twenty years, 65 per cent. between twenty and thirty, and 10 per cent. between thirty and forty years; 30 of the patients were white, 29 negroes.

For examination, the patient was placed in bed, with little clothing, to secure muscular relaxation and to give the best possible examination. To make the examination as nearly accurate as possible, they were made on the same day of the week and at the same hour in the day. Nine o'clock in the morning was the time chosen. An especial effort was made by palpating on the third day after labor to ascertain the effect produced by lactation upon the axillary and infraclavicular lymphatic glands. Most of the patients were examined but once after labor, some twice, and a few more frequently. When a pelvic infection like tuberculosis was present, the cases were excluded. All of the accessible lymphatic glands were examined except the popliteal. In the axillary it was noted whether the palpable glands were in the pectoral regions at the bottom of the axilla or in both regions. It was found useless to attempt to count definitely the number of glands in each region or group. The main question was to ascertain the size of the glands and, as far as possible, their consistence. Examinations were made independently of the patient's previous history. The patient, however, was questioned concerning the symptoms of tuberculosis of the glands, affections of the breasts, skin, teeth, scalp, sore throat, tonsillitis, and venereal disease.

The following is a summary of the results obtained: The total number of cases being 59, in but 1 of these patients could no glands be found upon examination. In none of the patients were the glands palpable in all the regions examined; in 98.3 per cent. of the cases, at some time the axillary glands could be distinguished; in the same percentage of cases the inguinal glands were also palpable at some time; in 74.6 per cent. the submaxillary glands could sometimes be felt; in 66.1 per cent. the axillary glands could be distinguished at every examination; in 62.7 per cent. the inguinal glands; in 44.2 per cent. the submaxillary glands; the supratrochlear were palpable in 30.5 per cent.; the posterior auricular in 10.1 per cent.; the superficial cervical glands in 5 per cent.; the suprahyoid in 1.7 per cent.; a progressive enlargement of the axillary glands was observed in 25.4 per cent.; in the inguinal 15.2 per cent.

Lactation caused enlargement of the axillary glands in 62.5 per cent. These glands could not be palpated in the second week of the puerperal period in one patient. Two weeks before delivery in one patient the axillary glands were enlarged and tender. After delivery the inguinal glands decreased in size in 21.6 per cent.

It was interesting to observe that the lymphatics were not symmetrical in the two sides of the body. The differences were greatest in the axillary, submaxillary, and supratrochear glands, and much less in the inguinal region. There were two patients in whom the glands could not be palpated.

The first was a white woman, aged twenty-nine years, the mother of five children. Her last labor was complicated by manual removal of the placenta. She had had children's diseases and an abortion, and the placenta had been manually removed at previous labors. This patient was under observation for seventeen days only. On two examinations no glands could be palpated.

The second case was that of a young negress aged sixteen years, rachitic, in whom no glands could be palpated on two successive examinations. During the third the right axillary glands were distinct, the inguinal glands barely perceptible. At the fourth examination the axillary and inguinal glands of both sides were palpable, but small. The axillary glands could not be detected sixteen days after labor, although the mother nursed her child. Four weeks after labor the inguinal glands of the right side could not be observed. The patient was delivered by pubiotomy, and the inguinal glands of the left side on which the operation was done were easily palpable. Engorged breasts invariably cause tenderness of the axillary glands, either before or after labor. Affections of the teeth or throat cause enlargement of the submaxillary glands. It could not be definitely decided whether the enlargement of the axillary lymphatics was due primarily to changes in the mammary glands or to pregnancy itself. In one case in which lobules of the mammary gland were found in the axilla, engorgement of the breasts was accompanied by sudden enlargement in the lymphatics. These glands decreased in size as the breasts grew smaller. Very often when lactation was developed the pectoral glands were strikingly enlarged, while those in the depths of the axilla were only slightly affected. It seems probable that the lymphatic glands of the whole body must be affected by pregnancy, but these changes are slight, gradual, and often transient, and enlargement which can be clearly detected seems to be caused by local conditions resulting from pregnancy.

The changes in the inguinal glands seem to be based primarily upon the results of pressure from the lower abdomen and pelvis. Age and multiparity seem to have no influence upon the lymphatic glands. Leucorrhœa before labor, injury at birth, obstetric operations, fever in the puerperal period, but not necessarily, produce changes in the lymphatics. In 1 case in which the child had ophthalmia, and the mother a well-marked leucorrhœa, the inguinal glands were enlarged three days after labor. This enlargement was temporary only, and soon disappeared.

We may explain the fact that the inguinal glands were not enlarged in patients that had tears in the perineum and vagina by aseptic and antiseptic methods employed at labor. It was observed that the inguinal glands were always more firm and flat than the axillary; the submaxillary were oval in shape and hard. The inguinal glands, however, undergo an early sclerosis, and possibly the changes in these glands had resulted from a previous venereal infection.

A comparison of the races shows that in the negress the lymphatic glands were larger in every region where they could be palpated. Progressive enlargement of the axillary glands was noted in 30 per cent. among negresses, and in 17 per cent. among the whites. These glands increased with beginning lactation more frequently among the negresses than the whites.

In giving his summary and conclusions, Meyer states the points already noted. He finds that no general enlargement of the lymphatic glands was observed in pregnancy. The enlargement noticed in the maxillary and submaxillary regions was due to local causes in the axilla and groin, induced by pregnancy; in the case of the submaxillary glands to the lesions of the teeth, gums, mouth, and throat. These

differences are thought to depend on the fact that the breasts were brought into active function, while the mouth, teeth, and scalp are very frequently neglected and the site of pathological conditions. In none of these cases could it be observed that new lymphatics developed during pregnancy.

GYNECOLOGY.

UNDER THE CHARGE OF

J. WESLEY BOVÉE, M.D.,

PROFESSOR OF GYNECOLOGY IN THE GEORGE WASHINGTON UNIVERSITY, WASHINGTON, D. C.

The Histological and Clinical Significance of Malignant Chorioepithelioma.—SCHMAUCH (*Surg., Gyn.,* and *Obst.,* 1907, v, 259) considers this subject very fully and declares that not always is chorioepithelioma malignant. Polano has expressed the belief, after a very careful analysis of all the cases of this disease in which successful operations had been performed, that 50 per cent. of the patients would have recovered without operation. Schmauch believes that every case of so-called surgical cure would have recovered spontaneously. He sums up as follows: The chorioepithelial proliferations described in literature as chorioepithelioma malignum have nothing in common with a malignant growth, as generally interpreted. On the other hand, the whole doctrine of chorioepithelioma proves a great support of Ribbert's theory of the development of carcinoma. Epithelial cell complexes, torn from their origin and deported, proliferate and form a kind of autonomous growth. There is only a gradual difference between the simple invasion of the uterine muscles by villi and their sequels, such as adherent placenta, the common and destructive placentary polyp, and the common and destructive mole; between the localized chorioepithelial growths, limited to the uterus and the placental region, and the villous infarcts, developed by deportation of villi; and finally between those cases in which the lungs are able to retain and master the scattered fœtal cells (mostly syncytial and atypical forms), and the typical chorioepithelioma malignum, which becomes generalized through general metastases. Only the latter two types deserve the name of malignant chorioepithelioma.

In recent publications concerning chorioepitheliomatous proliferations in the male, a tendency is to be noticed to regard those cases of generalized chorioepithelioma, in which the uterus and adnexa proved free from growth, as of teratoid genesis. However, as the connection with pregnancy is an established fact, we have no right to hunt for complicated theories. In many of the cases, in which the uterus was free from growth, a closer examination probably would have revealed smaller neoplastic foci in the parametrium. All the enumerated conditions are sequels of pregnancy. We deal with proliferations that trespass the physiological limits necessary for the development of the fertilized ovum and therefore become pathological. Fœtal cells and villi, which normally invade the uterine mucosa to bring about fixation of the ovum

and further development, pervade the musculature of the uterus, become deported into vaginal veins, and finally lead to the death of the bearer by general dissemination. Between the physiological embolism of placentary cells and the typical malignant chorioepithelioma there is only a gradual difference. Schmorl states expressly that small metastatic foci from a malignant chorioepithelioma cannot be differentiated microscopically from chorioepithelial embolism found in a vesicular mole.

Whether a badly nourished inferior mucosa facilitates the invasion of the villi, and leads to adherent placenta and placentary polyp or not, is mere speculation. Whenever villi have invaded intramuscular blood-vessels (not intravillous spaces), a deportation of villi or larger placentary cell complexes is rendered easy. When retrograde deportation in the external genitalia takes place, it will become manifest to the naked eye, and when deported into the lungs bloody expectoration will result. It is very probable that a number of the small-sized hematomas of the vulva and vagina, the so-called "thrombus vaginæ," are caused by villous infarcts. Older German text-books of obstetrics, for instance that of Spiegelberg, speak of such hematomas appearing during pregnancy, and some days after labor. While the development during labor was easily understood, in the other forms a friability of the bloodvessels was supposed to be the cause. It sounds strange to read reports of such patients, and hear of the protracted convalescences and of the grave alteration of the general conditions.

The so-called vaginal metastases, appearing after an operation, from which the patient recovers completely, seem at first sight absolutely malignant. They become easily understood, however, when one assumes that they were already deposited at the time of the operation, but did not become manifest until the insult, connected with the operative interference, led to the formation of a hematoma. The presence of villi in a villous infarct is not absolutely necessary for that diagnosis. They might become absorbed, or at other times it is possible that they will not be found. Among 11 cases classified by me as villous infarcts, villi were present 8 times.

When chorioepithelioma is regarded as a cellular injection and not as a true neoplasm, it will be useless to search for histological marks, proving malignancy or benignity. As the typical as well as the syncytial form may present all the different stages, we will never be able to render a definite opinion upon the eventful malignancy of the process from an extirpated vaginal nodule or uterus. The prognosis should always be guarded. As in bacterial infection, the seriousness of the invasion will be judged by the general, clinical symptoms, and not so much by the appearance of the diseased part of the body.

As the results become evident from the tabulation of the cases, only a few facts will be mentioned here: (1) The malignancy of the generalized chorioepithelioma and the prevalence of the typical chorioepithelioma among this class. (2) The lesser malignancy of the transition form syncytial chorioepithelioma (predominance of large syncytial cells besides Langhans' cells and syncytium). (3) The harmlessness of the atypical chorioepithelioma. Among the 206 tabulated cases, I find 10 which I regard as atypical chorioepithelioma consisting of large cells only, without admixture of Langhans'

cells and syncytium. 14 of them recovered after operation and 5 died. In 2 of these 5, sepsis is given as cause of death, in 1 nephritis, and in another one death soon followed the operation, while in the fifth the cause of death is not stated. There is so far not one case of generalization in an atypical chorioepithelioma reported. (4) The comparative benignity of all those cases in which villi were found in the extirpated uterus or in the vaginal infarcts. (5) While 43 cases of chorioepithelioma that proved to be malignant were preceded by abortion, only 24 followed molar pregnancy. Again, while 39 operated and recovered cases were preceded by mole, only 11 cases recovered after labor at term. On the other hand, 30 cases are recorded that died of malignant chorioepithelioma following full-term labor. Herewith is proved the frequency of chorioepithelial proliferation after mole and the danger of sepsis and exsanguination in destructive mole and placentary polyp, but not the histological malignancy of such relatively frequent proliferations. (6) The great importance of an exact anamnesis in judging the histological dignity of proliferations of the cells forming the cell-cover of villi.

Schmauch expresses great regret that gynecologists have considered the histology of so much greater importance than the symptomatology, which Schmauch considers should be reversed.

Postoperative Thrombosis and Embolism.—MILLER (*Amer. Jour. Obst.*, 1907, lvi, 347) classes the causes of postoperative thrombosis and embolism as follows: (1) Inflammatory thrombi, which are produced through acute or chronic inflammation of the wall of the heart or bloodvessels. As a consequence of the inflammation, the wall is thickened and the endothelium injured. (2) Traumatic thrombi produced through injuries to the vessel wall. To this classification belong those thrombi caused by ligation, severing, or tearing of the vessel. (3) Compression or dilatation thrombi, which are caused by slowing or stagnation of the blood stream. The compression can arise by the pressure of tumors, exudates, etc., and the dilatation may be due to actual disease, loss of elasticity, or excessive thinning of the vessel wall. Certain cardiac thrombi probably come under this head. (4) Marantic thrombi, which are due to diseased conditions of the blood, degeneration or weakness of the heart, and slowing of the blood stream.

Miller refers to the interesting experiments of Carrel and Guthrie on the anastomosis of bloodvessels and the transplantation of viscera as strongly indicating that infection and injury to the vessel wall are of primary importance etiologically. They found that in animals operated upon, in which the technique was rigid and the endothelium of the bloodvessels accurately adapted, thrombosis occurred but rarely. This does not explain the predilection of certain vessels to produce thrombi. Probably all the causes mentioned enter into most cases. Certainly they are most commonly formed when operations have been done for myoma or carcinoma of the uterus or ovarian tumors of prodigious proportions. Miller considers that the abnormal blood conditions notoriously present in these cases are the chief causes in them. He also lays stress upon the enlargement or dilatations of bloodvessels resulting from tumor pressure, as being a potent etiological factor, and he refers to the long oblique course of the iliac vein across the pelvis

behind the rectum and sigmoid flexure and the left iliac artery, as an explanation of the great frequency of involvement in thrombosis after operation. His paper is terminated by a statistical statement of the comparative frequency of involvement of various regional areas and structures.

Multiple Ovarian Cyst Successfully Removed from an Infant Aged Eleven Months.—C. W. MacGillivray (*Lancet*, 1907, i, 1487) reports the case of a girl of eleven months, whose mother, previous to the patient's birth, had 5 miscarriages. At the age of three months the child's abdomen was seen to be hard and large; at intervals the child suffered marked pain and had diarrhœal attacks. The abdomen increased in size rapidly and the child became more and more emaciated. Examination showed the child to be cyanosed and to have difficulty in breathing; the abdomen was enormously enlarged, the abdominal walls thin, and the umbilicus projected. The entire abdomen was dull to percussion. A puncture brought forth clear, yellowish fluid, and the relieved surface was found to be irregular and nodular. Operation revealed the condition to have been caused by a multilocular ovarian cyst attached at three points: below the liver, about the level of the umbilicus, and near the brim of the pelvis on the right side. These points contained large veins and arteries. The cyst was made up of two halves about equal in size and attached to each other by loose connective tissue. The length of the tumor was eleven inches, the thickness five. It filled up the whole distended abdominal cavity from the diaphragm to the true pelvis. The child recovered uneventfully.

Tubal Pregnancy Associated with an Ovarian Cyst.—E. G. E. Arnold (*Lancet*, 1907, i, 1490) reports the case of a woman upon whom he performed a laparotomy because of an ectopic gestation which was on the point of rupture; at the same time he found and removed an ovarian cyst the size of a tennis ball from the other side. The right tube and left ovary both appeared healthy and were therefore not disturbed. This tumor could not be found at an examination made nine months previously, and it has to be assumed therefore that it originated or at least grew very rapidly under the influence of the pregnancy.

Bacteriological and Clinical Examinations to Determine the Value of Modern Procedures in Performing Aseptic Gynecological Laparotomies. A large number of such examinations lead W. Hannes (*Zeit. f. Geburt. u. Gyn.*, 1907, lx, 1) to formulate the following conclusions. (1) Wounds produced during operations are constantly threatened with bacterial invasion from organisms on the hands of the operator and his assistants, from organisms on the skin of the patient, and from organisms floating in the air of the operating room. (2) Wearing dry, sterile rubber gloves on the disinfected dry hands makes the transference of bacteria from the hands of the surgeon completely impossible; this has been demonstrated repeatedly. (3) In a large number of instances, particularly in cases in which the operation lasts but a short time, it is unquestionably possible to keep the abdominal wall, which cannot be rendered absolutely aseptic, from coming in contact with the operative surface. Gaudanin is much more suitable for this purpose

than rubber dam; it particularly has many advantages over rubber cloth in those cases in which considerable fluid is constantly flowing over the abdominal coverings. (4) The possibility of an occasional infection from the air of the operating room is made likely by the result of bacteriological examinations. (5) Operative wounds known to contain bacteria may heal perfectly and promptly and do so very often. (6) When the technique is carried out rigidly even to the smallest details, the possibilities of errors and dangers is markedly lessened. (7) The use of a weak disinfecting fluid instead of the questionable normal saline solution for the purpose of rinsing the gloves seems an advantage; it were also better if the sterile instruments were kept in an antiseptic solution to protect them against the organisms in the air of the room. (8) The sterilizing apparatus should be examined bacteriologically from time to time. (9) Even when the most rigid technique thus far described is employed, it is impossible to assert, as has been done repeatedly within the last few years, that an absolutely germ-free operation can be performed.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.,

OF PHILADELPHIA.

Eruptive Sore Throat.—Edmund Cocks (*Jour. Amer. Med. Assoc.*, November 24, 1906) recently reported a case of pemphigus limited to the mucous membranes. The patient was a nervous woman, aged thirty-seven years, in the seventh month of pregnancy. For some months deglutition had been painful at the menstrual periods in consequence of numerous pea-sized vesicles on the tongue, buccal mucous membrane, pharynx, and lips. When seen by Dr. Cocks there was not a pea-size space of tongue, lips, buccal mucous membrane, pharynx or rhinopharynx that was not the site of vesicles. Vesicles were found on the conjunctiva, in the rectum, and in the vagina. The cervix was free. The patient died three weeks after confinement. Vesicles were found postmortem in the nares, mouth, tongue, pharynx, œsophagus, stomach, and intestinal tract from the pylorus to the anus. There were a few disseminated vesicles on the serous surface of the liver, spleen, intestines, and pleura. Cocks presumes the case to have been one of pemphigus limited to the mucous membranes, probably due to indican, the result of intestinal fermentation of several years' standing.

Hyperkeratosis of the Tonsils.—Geo. B. Wood. (*Annals of Otol., Rhin. and Laryng.* December, 1906) discusses and illustrates the etiology of hyperkeratosis of the tonsil, and places particular emphasis upon the importance of disassociating the leptothrix and other microörganisms as the causal factor.

Aberrant Tonsil.—CHAUVEAU (*Arch. internat. de laryng., d'otol., et de rhin.*, November and December, 1906) reports and pictures an aberrant hypertrophied tonsil behind the right posterior palatine fold in a man twenty-nine years of age, who had been sensible of discomfort for a few days only.

Resorption of Lymphoid Vegetations at the Vault of the Pharynx under the Influence of Infectious Disease.—To the few cases on record CHAUVEAU (*Arch. internat. de laryng., d'otol., et de rhin.*, November and December, 1906) adds an observation of rapid regression of adenoid vegetations in a case of measles in a child ten years of age; and he refers to three other cases of rapid regression under the influence of influenza, reported by him in *La france médicale*, September 1, 1899.

Fatal Syphilis of the Rhinopharynx.—FISCHENICH (*Verhand. des Verein Süddeut. Laryng.*, 1906) reports a case of syphilis of the rhinopharynx with fatal termination from repeated hemorrhages, in a man, forty years of age, who had acquired the initial disease some seven years previously.

Tuberculous Growth of the Pharynx.—SCHILLING (*Arch. internat. de laryng., d'otol., et de rhin.*, November and December, 1906) reports a tuberculous tumor at the vault of the pharynx, in a man fifty years of age, without tuberculosis in any other region. It was removed with an incandescent snare, and the remnants were destroyed with caustics. The patient had no trouble after the ablation of the growth.

Myxosarcoma of the Pharynx.—CALDEIRA CABRAL (*Arch. internat. de laryng., d'otol., et de rhin.*, September and October, 1906) reports the case of complete removal of adenoid vegetations from the pharynx of a young mulatto girl, ten years of age, who two months later presented similar symptoms with the addition of trismus and dysphasia.

Vegetations were felt behind the palate, and were removed by curetting. Histological examination revealed myxosarcoma. Recurrence ensued within ten days.

Extreme Congenital Stricture of the Œsophagus Successfully Relieved under Œsophagoscopy.—GUISEZ (*Annal. des maladies de l'oreille, du larynx, du nez, et du pharynx*, December, 1906) reports, among other cases, a remarkable one of extreme congenital stricture in a young man, eighteen years of age, who had never been able to take any nourishment but milk and water. The patient was being nourished through a gastric fistule which had been made for that purpose a short time previously. Under œsophagoscopy a large diverticulum at the inferior third of the œsophagus was found filled with mucus and curdled milk which, on aspiration with a pump amounted to a half litre. At the inferior portion of this pouch a sort of semilunar valve was observed obstructing the calibre of the œsophagus almost completely, and leaving but a very small orifice upon one side. This orifice barely admitted the smallest œsophageal bougie in the doctor's equipment.

In displacing the œsophageal tube toward the left, a sort of blind cul-de-sac of the left wall of the œsophagus was seen in which the bougies

were always caught in attempts at dilatation. Two months later this membrane was incised under œsophagoscopy after having been painted with a solution of adrenalin 1 to 1000, and then dilated with bougies of 4 and 6 mm., respectively. The patient was allowed to drink milk and gradually became able to take solids, so that at the end of three months he was able to eat any food, and had gained three pounds in weight. At the time of the report a bougie of 9 mm. could be passed.

Tuberculoma of the Nasal Septum.—A. ONODI (*Arch.. internat. de laryng., d'otol., et de rhin.*, November and December, 1906) reports a case of presumptive malignant growth of the nasal septum in a man sixty years of age. Thorough radical removal of the diseased septum and some adjacent structures was practised by external access, and the patient had an excellent recovery. Microscopic examination of the parts removed revealed tuberculoma of the nasal septum.

Tracheotomy Cannula in a Bronchus.—The dropping of an ill-cared-for tracheal cannula from electrolytic corrosion at the points of solder, where the contact of two metals and the corrosive liquid supply the conditions, has not been infrequent, especially before the practice of aseptic surgery. A recent case reported by M. JABOULAY (*Annales des maladies de l'oreille, du larynx, du nez, et du pharynx*, November, 1906), is illustrated with an unusually distinct *x*-ray reproduction showing the corroded cannula in the right bronchus. The foreign body was eventually removed under intra-oral bronchoscopy after failure of other methods, including resection of a rib; but, unfortunately, the patient died twelve days later of bronchopneumonia.

Gumma at the Bifurcation of the Bronchi.—J. GAREL (*Annales des maladies de l'oreille, du larynx, du nez, et du pharynx*, July, 1906) reports a case of gumma at the bifurcation of the bronchi detected by bronchoscopy. A characteristic ulceration of the superior upper border of the left Eustachian tube, which had not given any trouble whatever, had indicated the existence of syphilis, and the patient's cavernous, barking cough pointed to bifurcation or stenosis of the air passage, and thus led to the inspection by bronchoscopy.

Carcinoma of the Tongue and Larynx.—In reporting a case of modified transhyoid pharyngotomy with extirpation of the epiglottis, the upper third of the larynx, and the posterior two-thirds of the tongue. RICARDO BOTEY (*Archives internationales de laryngologie, d'otologie, et de rhinologie*, March and April, 1907) extols his modification of the procedure, which includes the partial resection of the hyoid bone and deep suturing of the tissues. The patient was a man, fifty-two years of age, and the morbid growth was found to be a squamous epithelioma. The extirpation was preceded by a tracheotomy six days previously. The main operation occupied more than two hours, but was not followed by shock and the patient made an excellent recovery, being apparently well with an intelligible speech and facile deglutition a month or so afterward.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

WARFIELD T. LONGCOPE, M.D.,

DIRECTOR OF THE AYER CLINICAL LABORATORY, PENNSYLVANIA HOSPITAL,

ASSISTED BY

G. CANBY ROBINSON, M.D.,

RESIDENT PHYSICIAN, PENNSYLVANIA HOSPITAL, PHILADELPHIA.

The Presence of Meningococcus and Micrococcus Catarrhalis in the Nasopharynx and Disinfection by Pyocyanase in these Infections.—Emmerich and Löw have made many observations upon the bactericidal action of pyocyanase toward such organisms as the cholera vibrio and diphtheria and typhoid bacilli, and they believe that the active principle of pyocyanase is a bacterolytic enzyme. Zucker has recently made use of pyocyanase as a local disinfectant in diphteria. JEHLE (*Wien. klin. Woch.*, 1907, xx, 8) finds that pyocyanase in dilute solutions is capable of inhibiting or destroying the growth of meningococci and of Micrococcus catarrhalis. It is much more active when added to pure cultures of these organisms than to exudates containing the cocci; for in the exudates many of the cocci are intracellular, and though pyocyanase rapidly dissolves the free cocci it does not attack the leukocytes. The property of pyocyanase as a disinfectant of the pharynx was then tested. An epidemic of grippe in a children's ward was found to be due to Micrococcus catarrhalis, which was often and repeatedly grown in pure cultures from the nasopharynx of the patients. One or two applications of pyocyanase in 0.5 to 3 c.c. doses were sufficient to destroy the organism, and cultures made subsequently never contained Micrococcus catarrhalis. Further, Jehle made cultures from the nasopharynx of 155 persons who were either suffering from meningitis or were in contact with meningitic patients. Cultures from 39 of these individuals gave growths of meningococci; sometimes in a pure state. After one or two instillations of pyocyanase, meningococci disappeared entirely from the nasopharynx. Jehle thinks that pyocyanase will prove a valuable disinfectant for the nose and throat of individuals infected with these two organisms. It is not useful for all bacteria, however, for experiments with streptococci, staphylococci, pneumococci, and the colon and the Friedländer bacillus gave poor or negative results.

Experimental Studies upon Acute Toxic Nephritis.—It has always been difficult to decide what one should call degenerations of the kidney and what nephritis. Ribbert restricts the term nephritis to those inflammations which involve the vessels and are accompanied by exudation and proliferative changes, and Friedrich Müller takes much the same view, suggesting the term nephrosis for the degenerative changes which affect the epithelium of both the tubules and glomeruli. Cohnheim, on the other hand, recognizes a true tubular nephritis. Aufrecht distinguishes two main types of nephritis: a variety in which the epithelium

of the tubules is affected, corresponding to the type of acute nephritis; and a variety in which the process is vascular and starts as a thickening of the walls of the vasa afferentia. Changes in the tubular epithelium occur later and the end result of this process is the "Schrumpfniere."

SCHLAYER and HEDINGER (*Deut. Arch. f. klin. Med.*, 1907, xl, 1) have made some interesting studies upon thes questions in rabbits poisoned by various substances. One of the important parts of the work was to measure the contraction and dilatation of the vessels by means of the Cohnheim-Ray oncometer. Variations in contraction and dilatation of the bloodvessels, and consequently the amount of blood in the kidney, were brought about in various ways. Under normal conditions after sensory stimuli the general blood pressure rose slightly and the vessels of the kidneys contracted; injections of adrenalin produced a greater rise in blood pressure and more marked contraction of the renal vessels. Injections of salt solutions and of caffeine did not give rise to any alteration of blood pressure, but caused an extreme grade of dilatation of the renal vessels which was accompanied by polyuria. Phloridzin produced glycosuria and polyuria without altering the blood pressure or the volume of the kidney.

In the first series of experiments nephritis was produced by poisoning the animals with chrome salts and with corrosive sublimate. These substances give rise to great destruction of the tubular epithelium without doing much damage to the glomeruli. The urine is plentiful, contains much albumin and enormous numbers of casts with detritus, but few blood cells. During the earlier stages of the intoxication the renal vessels, as measured by the oncometer, show normal or increased contraction following sensory stimuli and injections of adrenalin, and equally well-marked dilatation associated with polyuria and diuresis after injections of salt solution and caffeine. As the lesions in the kidney progress the vasodilatation and diuresis fail and after enormous destruction of the tubules with moderate changes in the glomeruli the vaso-dilatation and diuresis ceases almost completely though the power of vaso-constriction is well maintained. The reason for this gradual loss of vaso-dilatation was thought at first to be the mechanical hindrance of the dilatation of the vessels of the glomeruli from pressure brought to bear upon these structures by the casts in the tubules, but this was abandoned after it was found that during the early stages ligation of the ureter, a condition which would cause increased intratubular tension, did not interfere with the dilatation of the bloodvessels. The true explanation was found in the fact that the bloodvessels themselves were injured, proof of which was found in a second series of experiments. The nephritis in these experiments was brought about by the administration of cantharides, arsenic, and diphtheria toxin. With cantharides and arsenic the changes were the same. The anatomical lesions consisted principally in changes in the glomeruli. Moderate alterations were seen in the tubular epithelium, with casts in the tubules, but the glomeruli, especially in the severe cases, showed marked proliferation of the cells, with leukocytic infiltrations. The urine was scanty, contained relatively small amounts of albumin, great numbers of red blood cells, but only moderate number of casts. The changes in the contractility of the bloodvessels were entirely different from what was seen with the chrome salts and corrosive sublimate poisoning.

Even after small doses of cantharides and arsenic the power of dilatation of the vessels was almost entirely lost, and at the same time there was a disappearance of diuresis; with prolonged or more intense intoxication, total insufficiency of the renal vessels supervened and the elimination of the urine ceased almost entirely. These changes occurred with lesions in the kidney which did not approach in intensity the destruction following injections of sublimate and chrome salts.

Schlayer and Hedinger, from these experiments, distinguished two different types of acute nephritis: intoxication by chrome salts and corrosive sublimate causes a tubular nephritis, intoxication by cantharides and arsenic produces a vascular nephritis. Diphtheria toxin lies between the two, starting possibly as a tubular nephritis and ending certainly as a vascular nephritis. These experiments have, further, certain bearing upon the physiology of the kidney in general. It is evident that albumin can be eliminated from the glomeruli as well as from the tubular epithelium. The formation of casts has nothing to do with the bloodvessels, but takes place in the tubules. Every severe injury to the bloodvessels gives rise to a decrease in diuresis. With well-marked vessel changes phloridzin glycosuria no longer takes place. In extensive acute glomerular nephritis the function of the entire vascular system of the kidney is destroyed. Vascular nephritis is accompanied in its acute course by a low blood pressure, which may be due to the fact that the entire vascular system is injured by the poison producing the particular form of nephritis.

A Complex Hemolysin of the Pancreas.—Friedemann (*Deut. med. Woch.*, 1907, xxx, 585) finds that the fluid from a pancreatic fistula in animals contains a hemolysin which may be activated by lecithin, and which is comparable to the lecithins of the venoms of snakes and the poisons of bees. The pancreatic gland, moreover, contains a complex hemolysin which may be extracted with alcohol. This hemolytic substance may be activated by blood serum or by the alcoholic or ethereal extract of blood serum, but it cannot be activated by lecithin. It acts like an amboceptor, inasmuch as it is bound to the red blood corpuscles at a temperature of 0° C., but differs from an amboceptor in its high degree of thermolability. Small amounts of this pancreatic extract are capable of deviating the complement; and this power and the hemolytic power seem to be combined in one and the same substance. The substance is autohemolytic. Besides these properties the extract of the pancreas contains a toxin and a hemorrhagic poison which are similar in their action to crotalus toxin.

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All communications should be addressed to—

Dr. A. O. J. Kelly, 1911 Pine Street, Philadelphia, U. S. A.